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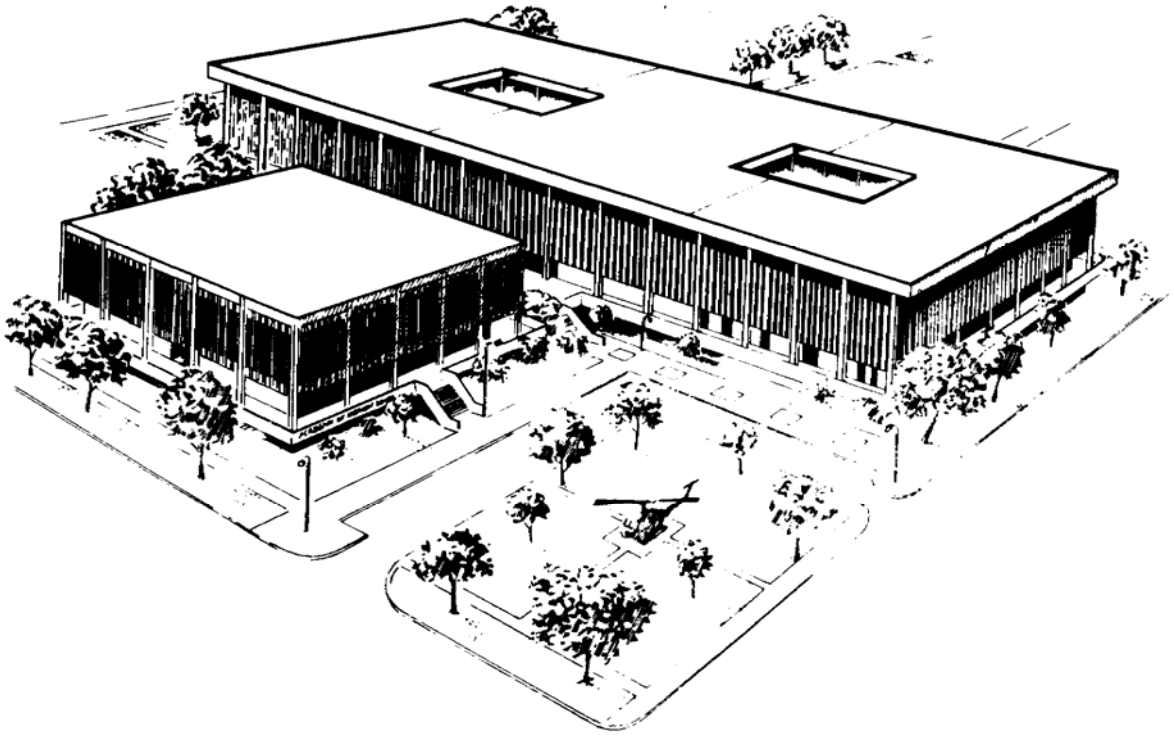
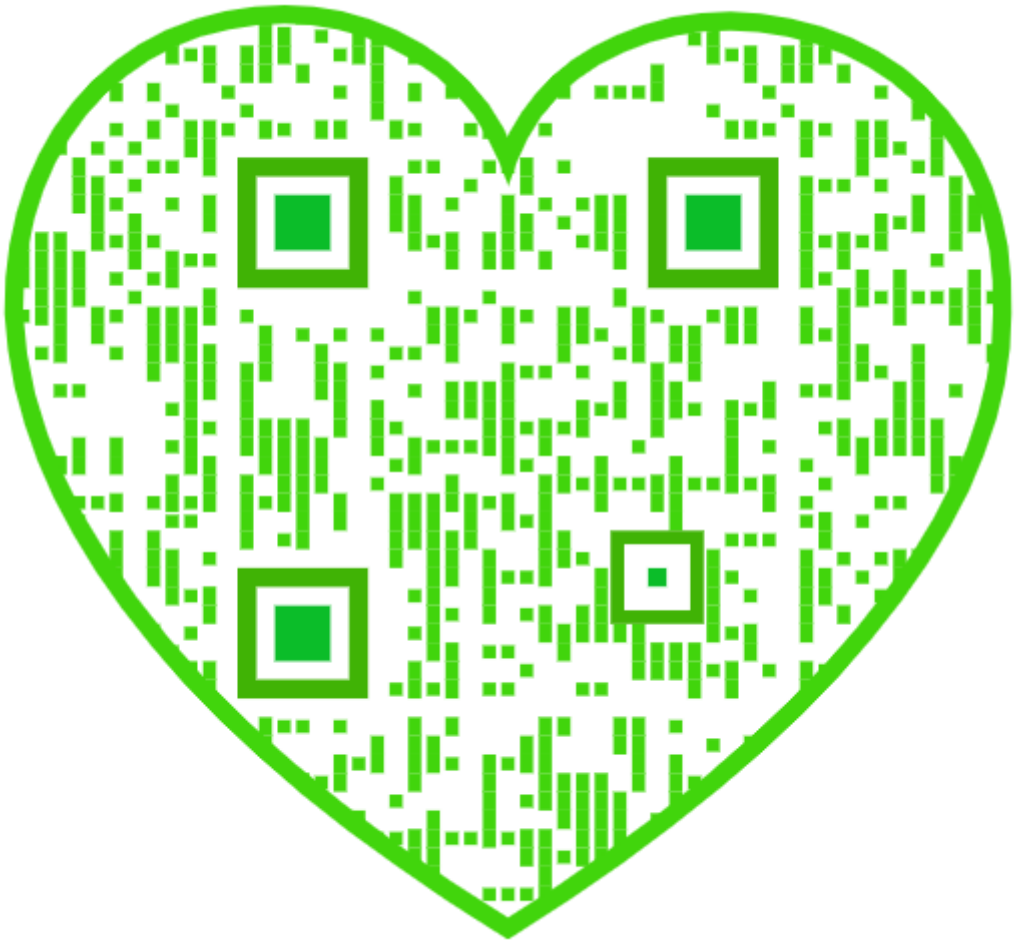
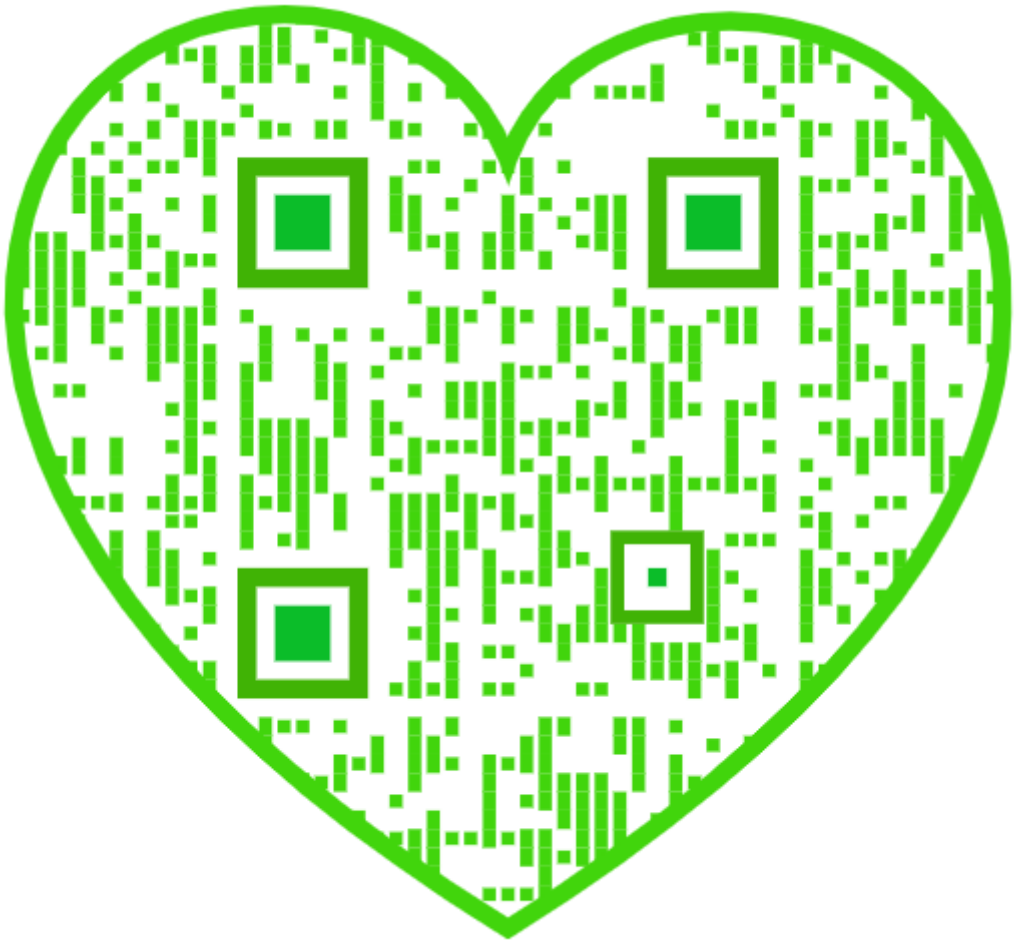


THERAPEUTICS I

SUBCOURSE MD0804 EDITION 200





DEVELOPMENT

This subcourse is approved for resident and correspondence course instruction. It reflects the current thought of the Academy of Health Sciences and conforms to printed Department of the Army doctrine as closely as currently possible. Development and progress render such doctrine continuously subject to change.

ADMINISTRATION

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CLARIFICATION OF TRAINING LITERATURE TERMINOLOGY

When used in this publication, words such as "he," "him," "his," and "men" are intended to include both the masculine and feminine genders, unless specifically stated otherwise or when obvious in context.

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USE OF PROPRIETARY NAMES

The initial letters of the names of some products are capitalized in this subcourse. Such names are proprietary names, that is, brand names or trademarks. Proprietary names have been used in this subcourse only to make it a more effective learning aid. The use of any name, proprietary or otherwise, should not be interpreted as an endorsement, deprecation, or criticism of a product; nor should such use be considered to interpret the validity of proprietary rights in a name, whether it is registered or not.

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CORRESPONDENCE COURSE OF
U.S. ARMY MEDICAL DEPARTMENT CENTER AND SCHOOL

SUBCOURSE MD08O4

THERAPEUTICS I

INTRODUCTION

A patient who visits a physician or physician extender frequently receives a prescription for a medication. That prescription is brought to the pharmacy to be filled. The patient expects professional attention at the pharmacy. Part of that expectation involves any caution or warning the patient should heed while taking the medication.

In your role, you will serve as a source of drug information. Patients and friends will ask you specific questions concerning the use of prescription and over-the-counter medications. You must know the trade and generic names of literally hundreds of medications. Furthermore, you must know the cautions and warnings associated with many agents.

How are you to know this information about drugs? Certainly you have had instruction which presented the basics of anatomy, physiology, and pharmacology. This instruction has given you a sound foundation for learning more in these areas. This subcourse will present instruction in anatomy, physiology, and pharmacology. The material in anatomy and physiology is included to refresh your memory or to give you additional information so you can better understand the pharmacology material.

This subcourse is not intended to be used as an authoritative source of drug information. As you know, new drugs are constantly being discovered and new uses for existing drugs are being found through research. Therefore, you must rely upon this subcourse to review concepts or to learn new information. You are then to use other sources (see lesson 1 of this subcourse) to gain new information as it is discovered.

Subcourse Components:

This subcourse consists of 11 lessons. The lessons are:

Lesson 1. Professional References in Pharmacy.
Lesson 2. Anatomy, Physiology, and Pathology Important to Therapeutics.
Lesson 3. Introduction to Pharmacology.
Lesson 4. Local Anesthetic Agents.
Lesson 5. The Central Nervous System.
Lesson 6. Agents Used During Surgery.
Lesson 7. Sedative and Hypnotic Agents.
Lesson 8. Anticonvulsant Agents.

Lesson 9. Psychotherapeutic Agents.
Lesson 10. Central Nervous System (CNS) Stimulants.
Lesson 11. Narcotic Agents.

--Read and study each lesson carefully.

--Complete the subcourse lesson by lesson. After completing each lesson, work the exercises at the end of the lesson

--After completing each set of lesson exercises, compare your answers with those on the solution sheet that follows the exercises. If you have answered an exercise incorrectly, check the reference cited after the answer on the solution sheet to determine why your response was not the correct one.

Credit Awarded:

Upon successful completion of the examination for this subcourse, you will be awarded 14 credit hours.

To receive credit hours, you must be officially enrolled and complete an examination furnished by the Nonresident Instruction Section at Fort Sam Houston, Texas.

You can enroll by going to the web site http://atrrs.army.mil and enrolling under "Self Development" (School Code 555).

LESSON ASSIGNMENT

LESSON 1	Professional References in Pharmacy.
TEXT ASSIGNMENT	Paragraphs 1-1 through 1-8.
LESSON OBJECTIVES	1-1. Given a description of a reference used in pharmacy and a list of pharmacy references, select the particular reference being described.
	1-2. Given a description of a situation requiring the use of a pharmacy reference and a list of pharmacy references, select the reference most likely to contain the information required in that situation.
SUGGESTION	After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 1

PROFESSIONAL REFERENCES IN PHARMACY

Section I. GENERAL

1-1. CONSIDERATIONS INVOLVED IN SELECTING A REFERENCE

a. At this point, you may already possess a strong background in pharmacology. However, if you do not take steps to maintain and expand your knowledge in pharmacology, you will quickly find yourself out-of-date in terms of drugs and drug therapy. Furthermore, no individual knows everything about every drug used in medicine. What happens when a drug-related question arises? What sources of drug information should be readily available in the pharmacy? Which reference should be consulted to find the answer to a specific question? These questions will be examined in this lesson.

b. This lesson does not attempt to every available pharmaceutical reference. Instead, this lesson will focus on some references that are commonly used in the practical of pharmacy.

c. Some references, by design, are tailored to meet the needs of those persons who have strong backgrounds in pharmacy, physiology, and/or medicine. Therefore, you should carefully select references that are written to a level comparable to your background and experience. An individual who lacks a technical background can become frustrated when reading a highly technical reference.

1-2. HUMAN SOURCES

Use human sources of information. Most health care professionals are more than willing to share their knowledge and experience. Carefully identify those professionals who are willing to instruct you and/or answer your questions. Also, you should be willing to share your knowledge and experience with others.

Section II. PHARMACEUTICAL JOURNALS

1-3. OVERVIEW

a. Journals serve as excellent sources of drug information. For the most part, the information contained in journals is up-to-date. Journals reflect the state of the art of that discipline at that point in time.

b. Some journals are designed to be read by many members of the medical community. Other journals are specifically written to meet the needs of the individuals who are directly involved with the field of pharmacy. Further, some journals are especially written for pharmacy personnel, who work in hospitals, while others are designed for those who work in retail.

c. As you know, there are many journals written for people who work in the medical field. Some journals are designed to be read by the members of many medical disciplines, while other journals focus on a particular job specialty (that is, nursing, pharmacy, or medical technology). Many journals are written to meet the needs of those in pharmacy practice. Some of these journals are especially written for pharmacy personnel who work in an inpatient setting, while other journals are designed for those who work in an outpatient environment.

d. To meet your individual needs, you should become familiar with some frequently used pharmacy journals, the type of information each contains, and the particular group(s) for whom the journal is written.

e. As you read a journal, do not limit yourself to the main articles. Letters to the editor, advertisements, and job announcements also provide information, which can be very helpful. For example, these parts of a journal can provide up-to-date information on new products, changes in old products, as well as short- and long-term trends in the state of the art of pharmacy practice.

1-4. SPECIFIC JOURNALS

a. **The American Journal of Health-Systems Pharmacists**. The American Journal of Health-Systems Pharmacists (AJHP) is an official publication of the American Society of Health-Systems Pharmacists. It is published on a twice monthly basis. As the name implies, this journal is tailored to pharmacy personnel who practice in a hospital setting. The AJHP can be read and understood by almost all-medical personnel who have a background in pharmacy. The AJHP contains information on drug therapy, new and innovative pharmacy practices, and other topics of particular interest to hospital pharmacy personnel.

b. **Hospital Pharmacy**. This journal is a monthly publication of the L. B. Lippincott Company. Although designed for hospital pharmacists, the journal's contents can be read and understood by medical personnel who have a background in pharmacy. Hospital Pharmacy contains information on innovative pharmacy procedures (that is, unit dose), drug therapies, and other topics of general interest. One section, "Medication Error Reports," provides a constant reminder of the types of medication errors that occur in a hospital.

c. **The American Journal of Intravenous Therapy.** The McMahon Publishing Company on a bimonthly basis publishes this journal. The journal is tailored toward those persons directly involved with the preparation and/or administration of intravenous products. Therefore, it is particularly useful to the pharmacy personnel who work in the unit-dose/sterile product area. Experienced sterile product prepares should be able to read and understand this journal. Articles in this journal focus on the theoretical and practical considerations of intravenous therapy.

d. **American Pharmacy.** This journal is the official publication of the American Pharmaceutical Society. It is published on a monthly basis. It is especially designed for pharmacists who work in an outpatient environment, although the journal contains useful information for all pharmacy personnel. Articles in American Pharmacy cover a variety of pharmacy-related topics. For example, changes in drug laws, changes in drug therapies, and perspectives on the various aspects of health-care management are found in the journal

e. **Clinical Pharmacology and Therapeutics.** This journal is the official publication of the American Society for Clinical Pharmacology and Therapeutics and the American Society for Pharmacology and Experimental Therapeutics. As the name implies, the journal is designed to communicate up-to-date drug information and research related to pharmacology to those medical personnel who have an in-depth background in pharmacology, therapeutics, and the basic sciences.

f. **The Journal of Clinical Pharmacology.** This journal is the official publication of the American College of Clinical Pharmacology. This publication is designed for those medical personnel who have an excellent background in pharmacology, therapeutics, and the basic sciences. Articles focus on clinical research pertaining to pharmacology.

Section III. PHARMACEUTICAL TEXTS

1-5. OVERVIEW

As with journals, many texts are available to pharmacy personnel. Some texts require a certain amount of background knowledge in physiology, anatomy, and/or pharmacology. It is important for you to recognize your background strengths and weaknesses before you begin to search for a text to answer a particular question. You should also be familiar with the subjects discussed in each of these texts. Being able to identify a text on your knowledge level, which can provide you with the answer you are seeking, can pay dividends in terms of saved time and reduced frustration.

1-6. SPECIFIC TEXTS

a. **The Physicians' Desk Reference.** The Physicians' Desk Reference (PDR) is published on an annual basis by the Medical Economics Company. The drug manufacturers, whose products are listed in the reference, prepare the information contained in the PDR. For the most part, the drug monographs in the PDR come directly from the package inserts for the drugs. The publisher supplies periodic supplements to the text. The PDR is written primarily for physicians; however, many medical personnel have the background to use the reference. The PDR is divided into the following nine areas:

(1) The Manufacturers' Index. This section supplies information (that is, address and telephone number) on the manufacturers who supplied prescribing information for the PDR.

(2) The Product Name Index. This section provides an alphabetical listing of the drug products by trade name and the page number where the drug product information may be located.

(3) The Product Classification Index. This section of the PDR provides an alphabetical listing of the drug products by their therapeutic classifications. Page numbers for locating the drug products are provided for quick reference.

(4) The Generic and Chemical Name Index. In this section, the products are categorized under generic and chemical name headings according to their principal components.

(5) The Product Identification Section. This section of the PDR provides a pictorial display (by manufacturer) of capsules, tablets, and containers. This area can be used to identify products that one does not immediately recognize by appearance.

(6) The Product Information Section. Manufacturer lists this alphabetical arrangement of over 2,500 pharmaceuticals. The drug products are fully described in the following areas: common names, generic compositions, chemical names, composition, action and uses, administration and dosage, contraindications, precautions, side effects, supplied, and other information concerning use.

(7) The Diagnostic Product Information Section. The PDR focuses on the descriptions of diagnostic products. This section of PDR focuses on the descriptions of diagnostic products. The products are listed alphabetically.

(8) The Poison Control Centers Section. This section contains a list of poison control centers and their emergency telephone numbers.

(9) The Guide to Management of Drug Overdose Section. This section is located on the inside back cover of the PDR. The aim of this section is to provide the physician with useful information on the management of drug overdoses. Of course, any individual who is suspected to have ingested an overdose of medication should be taken to the nearest medical treatment facility for prompt attention and treatment.

b. **Remington's Pharmaceutical Sciences.** Mack Publishing Company publishes this text. Although written for pharmacists, who work in any pharmacy setting, the reference can be read, understood, and used by other medical/pharmacy personnel. Remington's deals with the theory and practice of the art of pharmacy. It provides essential information about drugs. Furthermore, the text is especially useful as an information source for the compounding of extemporaneous products.

c. **The Pharmacological Basis of Therapeutics**. Louis Goodman and Alfred Gilman wrote this text. This reference is written for medical personnel who have a strong background in physiology and pharmacology. Indeed, it is not written for a reader who has a weak or limited background in the sciences. The clinical application of drug knowledge is the aim of the text. The book is divided into major sections based upon therapeutic categories. Sections are subdivided into chapters that focus on specific drug uses. Each chapter has an excellent overview of the therapeutic area and a discussion of considerations pertinent to the topic being examined.

d. **American Medical Association Drug Evaluations.** The American Medical Association (AMA) Department of Drugs prepares this text. The book is written on a level that can be read and understood by medical personnel who have a good background in physiology and pharmacology. American Medical Association Drug Evaluations is divided into sections based upon therapeutic classifications. Each chapter has an introductory statement that discusses considerations involved with that therapeutic category. Further, each chapter contains informative monographs on drugs pertinent to that category. Dosage information is provided under each drug monograph.

e. **Drug Interactions**. Philip D. Hansten wrote this text. It is written for the health-care provider who is concerned about drug interactions and/or the effects upon clinical laboratory tests by specific agents. Section one of the book is divided into chapters based upon drug interactions of particular therapeutic categories. Section two deals with the impact of certain medications upon specific clinical laboratory test results.

f. **Dorland's Illustrated Medical Dictionary**. W. B. Saunders Company publishes this reference. This medical dictionary is a useful reference for all medical personnel. In particular, the dictionary can be used by pharmacy personnel whenever unfamiliar medical terms are encountered.

g. **Handbook of Injectable Drugs**. This book was written by Lawrence A. Trissel. It is especially tailored to meet the needs of pharmacy personnel who are directly involved with the preparation of intravenous admixtures. The text is easily used; however, care should be exercised when using the charts provided in the reference. The drugs listed are limited to injectable products. For each drug, a monograph is provided which includes information on drug concentration, stability, pH, dosage, compatibility, and incompatibility.

h. **The American Hospital Formulary Service**. The American Hospital Formulary Service (AHFS) is a two-volume collection of drug monographs published by the American Society of Health-Systems Pharmacists. The AHFS is designed to be used by all pharmacy personnel. It is divided into sections based upon therapeutic categories. A general statement pertaining to the therapeutic category is included at the beginning of each individual section. Individual drug monographs that present information on drug chemistry, dosage, and preparations follow this general statement. Information on the drug monographs is kept current by periodic supplements to the AHFS.

i. **The American Drug Index**. Norman Billups writes the American Drug Index (ADI). The book is designed to provide information to all medical personnel in general and to pharmacy personnel in particular. The monographs contained in the ADI are listed in alphabetical order. Both trade and generic names are provided. The monographs in the ADI do not provide information on actions and dosage. Instead, specific information (that is, manufacturer, amount of each ingredient present in the dosage form and the use of the drug) is provided for each product listed.

j. **Pharmaceutical Calculations.** Mitchell J. Stoklosa wrote this reference. It was designed for use as a calculation text. Although it is not a pharmacology text, it is useful to rely on such a reference when questions on dosage calculations arise. Periodic review of calculation concepts is helpful to all pharmacy personnel.

k. **Facts and Comparisons**. Facts and Comparisons, Inc wrote this reference. It is designed to be used by most medical personnel in general and by pharmacy personnel in particular. Facts and Comparisons are organized into twelve main chapters by drug use. Drugs and/or drug products are listed together in such a way as to provide rapid comparisons between drugs or products that are similar in use or content. Individual drug monographs provide comprehensive information on drug actions, contraindications, warnings and precautions, drug interactions, adverse reactions, over-dosage, and administration and dosage. The publisher provides monthly updates of this loose-leaf text. These updates ensure that the most recent information on new products and developments in drug therapy are available to the reader. Moreover, the publisher has available a slide-tape presentation which provides information on the use of the reference.

l. **Handbook of Poisoning: Diagnosis and Treatment**. This text was written by Dr. Robert H. Dreisbach and published by Lange Medical Publications. This reference provides a concise summary of the diagnosis and treatment of many poisons. The book is divided into chapters that discuss such topics as general considerations (that is, prevention and management), agricultural poisons, industrial hazards, household hazards, medicinal poisons, and animal and plant hazards. Information on first-aid measures is found on the front and back covers of the text.

m. **The United States Pharmacopoeia and The National Formulary**. The United States Pharmacopoeia and The National Formulary reference contains standards and tests for quality, purity, strength, packaging, and labeling of drugs in the United States. This reference is designed to be used by researchers and pharmacists who are concerned about the standards that have been established for drugs. The United States Pharmacopoeia and The National Formulary reference has information that is useful for personnel who are involved in both inpatient and outpatient pharmacy practice. Annual supplements to the reference ensure that it contains the latest information on the state of the art of pharmacy.

n. **United States Pharmacopoeia Dispensing Information**. The United States Pharmacopoeia Convention, Inc publishes the United States Pharmacopoeia Dispensing Information annual publication. This reference is designed to be used by individuals who dispense drugs and by persons who administer drugs after the drugs have been prescribed. The following information about a drug is discussed in the text: category of use, precautions to use, (that is, drug interactions and medical warnings), drug preparation immediately prior to administration, side effects with an indication of their significance, guidelines for patient consultation on safe and effective use of the drug, dosing information, and requirements for packaging and storage. One section, "Advice for the Patient," provides guidelines for patient use of the drug. These guidelines are written in lay terms. Bimonthly updates keep the information in the United States Pharmacopeial Dispensing Information current.

Section IV. ELECTRONIC DRUG INFORMATION SERVICES

1-7. OVERVIEW

As with journals and texts, electronic forms of drug information are now available to pharmacy personnel. Most of the reference texts discussed previously are available on CD Rom for single or network use. Some examples are Facts and Comparisons, the PDR, and Clinical Pharmacology. The advantages of this form of information include easy access to information and timely updates (monthly, quarterly, semiannually). Micromedex® is another information system available as a subscription at most military pharmacies. Micromedex® provides drug information monographs, drug identification (Identidex®), poison information (Poisindex®), material safety data sheets, Martindale's Extra Pharmacopeoia, AfterCare Notes®, as well as many other options. The majority of these systems are user friendly and easy to use with minimal orientation.

1-8. ELECTRONIC JOURNALS

The most current information about drug use, even prior to approval by the Food and Drug Administration, is available in medical journals. Medical journals are accessed through on-line searches such as Medline® and Grateful Med®. Many U.S. medical teaching institutions and major medical centers offer search capabilities via the Internet or through their respective medical libraries. The use of on-line information services often requires a thorough orientation to perform a good search.

Continue with Exercises

EXERCISES, LESSON 1

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. A friend has brought several capsules for you to identify; however, at first glance you are unable to name the particular medication. Select, references below, the reference you would use to identify the capsule.

   a. The Physicians' Desk Reference.

   b. Dorland's Illustrated Medical Dictionary.

   c. The United States Pharmacopoeia and the National Formulary.

2. Select, from the list below, the reference that deals with the theory and practice of the art of pharmacy. It is especially useful as an information source for the extemporaneous compounding of products.

   a. The Pharmacological Basis of Therapeutics.

   b. The United States Pharmacopoeia Dispensing Information.

   c. The American Hospital Formulary Service.

   d. Remington's Pharmaceutical Sciences.

3. Select, from the list below, the journal that focuses on the sterile products/unit-dose area of the hospital pharmacy.

   a. The American Journal of Health-Systems Pharmacists.

   b. Hospital Pharmacy.

   c. The American Journal of Intravenous Therapy.

   d. American Pharmacy.

4. Select, from the references below, the journal tailored to meet the needs of pharmacy personnel whose practice is in a hospital setting. This journal contains information on drug therapy and new and innovative pharmacy practices.

   a. The American Journal of Intravenous Therapy.

   b. The American Journal of Health-Systems Pharmacists.

   c. The Journal of Clinical Pharmacology.

   d. American Pharmacy.

5. Select, from the list below, the journal that primarily contains articles related to clinical research in pharmacology.

   a. The Journal of Clinical Pharmacology.

   b. American Pharmacy

   c. The Pharmacological Basis of Therapeutics.

   d. Hospital Pharmacy.

6. Select, from the list below, the journal that is tailored to meet the needs of pharmacists who work in an outpatient pharmacy environment.

   a. The Journal of Clinical Pharmacology.

   b. Clinical Pharmacology and Therapeutics.

   c. The Physicians' Desk Reference.

   d. American Pharmacy.

7. You have a question pertaining to the effect upon a particular laboratory test by a specific medication. From the list below, select the reference most likely to provide you the information you need.

   a. America Medical Association Drug Evaluation.

   b. Drug Interactions.

   c. Handbook on Injectable Drugs.

   d. Remington's Pharmaceutical Sciences.

8. During your reading of a journal article, you encounter the word "retroinfection." From the references below, select the reference you would use to find the meaning of that term.

   a. Dorland's Illustrated Medical Dictionary.

   b. America Medical Association Drug Evaluations.

   c. Remington's Pharmaceutical Sciences.

   d. Handbook on Injectable Drugs.

9. A friend of yours is concerned about the safety of his children. It seems that he believes he has many poisonous plants and chemicals in his home. From the list below, select the reference most likely to give him the information he needs.

   a. Facts and Comparisons.

   b. The American Hospital Formulary Service.

   c. Handbook of Poisoning: Diagnosis and Treatment.

   d. The American Drug Index.

10. Select, from the list below, the reference that contains a section, which provides pharmacy personnel with specific information that should be communicated to the patient concerning the use of a particular drug.

    a. The American Drug Index.

    b. Handbook of Poisoning: Diagnosis and Treatment.

    c. The Pharmacological Basis of Therapeutics.

    d. The United States Pharmacopeia Dispensing Information.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 1

1. a (para 1-6a)
2. d (para 1-6b)
3. c (para 1-4c)
4. b (para 1-4a)
5. a (para 1-4f)
6. d (para 1-4d)
7. b (para 1-6e)
8. a (para 1-6f)
9. c (para 1-61)
10. d (para 1-6n)

End of Lesson 1

LESSON ASSIGNMENT

LESSON 2 Anatomy, Physiology, and Pathology Important to Therapeutics.

TEXT ASSIGNMENT Paragraphs 2-1 through 2-20.

LESSON OBJECTIVES After completing this lesson, you should be able to:

2-1. Given a term pertaining to anatomy, physiology or pathology and a group of definitions, select the definition of that term.

2-2. Given the name of a system of the body and a group of functions, select the function of that system.

2-3. Given the name of a structural component of a cell and a group of descriptions, select the most appropriate description of that structure.

2-4. Given the name of a type of tissue and a group of descriptions, select the most appropriate description of that type of tissue.

2-5. Select from a list of functions the function of the skin.

2-6. Given the name or type of a disease of the skin and a group of descriptions, select the best description of that particular disease.

2-7. Given a cause of disease and a group of statements discussing various causes of disease, select the statement that best describes that cause.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 2

ANATOMY, PHYSIOLOGY, AND PATHOLOGY IMPORTANT TO THERAPEUTICS

Section I. PRINCIPLES OF ANATOMY AND PHYSIOLOGY

2-1. ANATOMY AND PHYSIOLOGY

a. Anatomy is the study of the structure of the body. Often, you may be more interested in functions of the body. Functions include digestion, respiration, circulation, and reproduction. Physiology is the study of the functions of the body.

b. The body is a chemical and physical machine. As such, it is subject to certain laws. These are sometimes called natural laws. Each part of the body is engineered to do a particular job. These jobs are functions. For each job or body function, there is a particular structure engineered to do it.

c. In order to read and understand basic concepts in pharmacology, you must be familiar with certain topics in anatomy, physiology, and pathology. It is not the intent of this subcourse to discuss these areas in detail. Instead, the content of this lesson should give you the knowledge required to complete this subcourse. If you want, you can read texts and references that discuss these areas in detail.

2-2. ORGANIZATION OF THE HUMAN BODY

The human body is organized into cells, tissues, organs, organ systems, and the total organism.

a. Cells are the smallest living unit of body construction.

b. A tissue is a grouping of like cells working together. Examples are muscle tissue and nervous tissue.

c. An organ is a structure composed of several different tissues performing a particular function. Examples include the lungs and the heart.

d. Organ systems are groups of organs, which together perform an overall function. Examples are the respiratory system and the digestive system.

e. The total organism is the individual human being. You are a total organism.

2-3. SYSTEMS OF THE BODY

A system is a combination of parts or organs, which, in association, perform some particular function. The systems of the body are as follows:

a. **Integumentary.** Covers and protects the body from drying, injury, and infection, and has functions of sensation, temperature regulation, and excretion.

b. **Skeletal.** Provides a framework for the body, supports the organs, and furnishes a place of attachment for muscles.

c. **Muscular.** Provides the force for the motion and propulsion of the body.

d. **Respiratory.** Absorbs oxygen from the air and gives off the carbon dioxide produced by the body tissues.

e. **Cardiovascular.** Functions in the transportation of blood throughout the body.

f. **Lymphatic (System of Vessels and Glands).** Returns protein and fluid to the blood from the various body tissues; also furnishes the body with protective mechanisms against pathogenic organisms.

g. **Gastrointestinal**. Digests and absorbs food substances and excretes waste products.

h. **Genitourinary.** Excretes and transports urine (urinary), and elaborates and transports reproductive cells and sex hormones (reproductive).

i. **Nervous and Special Senses**. Gives the body awareness of its environment, and enable it to react to that environment.

j. **Endocrine.** Manufactures hormones, which are active in the control of much of the body activity and behavior.

Section II. CELLS

2-4. INTRODUCTION

Each of the 100 trillion cells in a human being is a living structure that is capable of surviving indefinitely. In most instances, the cell can reproduce itself provided its surrounding fluids remain intact. To understand the function of the various organs and other structures of the human body, it is essential that you first understand the basic organization of the cell and the functions of its component parts.

2-5. STRUCTURAL COMPONENTS OF A CELL

The cell was once viewed as a bag of fluid, enzymes, and chemicals. Now, we understand that the cell is an extremely complex living the entity. With the advent of electron microscopy in the early 1940's, several distinct cellular structures called organelles were clearly recognized. A typical animal cell contains several types of these organelles. Each organelle has an important role in the functioning of the cell. It is important for you to become familiar with these organelles.

a. **Cell Membrane.** Animal cells do not have cell walls; they have cell membranes (figure 2-1)only. Plant cells have both cell walls and cell membranes.

(1) Practically all the structures within the cell, as well as the cell itself, are lined with a porous, elastic membrane. The cell membrane is composed primarily of lipids (fats) and proteins that are arranged in layers at right angles to each other (figure 2-1).

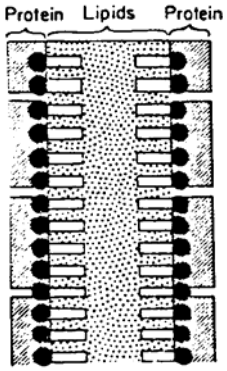


Figure 2-1. Diagram of a cell membrane.

(2) The lipids of the cell wall are composed of two portions: a long hydrocarbon chain (that is insoluble in water) and a glycerol-phosphate head (that is soluble in water). The long chains are in the center of the protein and the glycerol-phosphate group is attached to the end of the protein.

(3) The cell membrane contains many pores. It is through these pores that lipid-insoluble particles, such as water and urea, pass between the interior and the exterior of the cell. Diffusion experiments have shown that particles up to approximately 8-Angstrom units in diameter pass through the pores freely.

(4) The main function of the cell membrane is to regulate the flow of substances into and out of the cell. This regulation of flow is accomplished by the membrane's selective permeability. That is, only certain substances may pass through the pores. This is important, since the cell must obtain the nutrients for its growth from the extracellular fluid (fluid outside the cell) and discard waste products back into the extracellular fluid.

b. **Cytoplasm.** Cytoplasm (figure 2-2) is the fluid or semifluid contained inside the cell membrane, but outside the nucleus. The cytoplasm functions as a medium to contain many substances, such as fats, glucose, proteins, water, and electrolytes. The clear portion of the cytoplasm is called hyaloplasm. Located within the cytoplasm are the organelles that perform highly specialized functions in the cell.

c. **Nucleus**. The nucleus (figure 2-2) is the control center for the cell. It controls the reproduction of the cell as well as the chemical reactions that occur within the cell. The nucleus contains large amounts of deoxyribonucleic acid (DNA). The DNA is responsible for controlling the characteristics of the protein enzymes of the cytoplasm, and thus, it controls cytoplasmic activities. The DNA is also responsible for controlling the hereditary characteristics of individuals.

d. **Mitochondria**. The mitochondria (figure 2-2) may be called the power house" of the cell. The mitochondria are the site of cell respiratory activity. The mitochondria are found in the cytoplasm. They are usually located near energy requiring structures (that is, nodes of nerves, contracting ligaments of muscles, active transport mechanisms in membranes and ribosomes). Their numbers depend on the amount of energy required by the cell to perform its function. Several infoldings of the inner unit membrane form shelves on which practically all of the oxidative enzymes of the cell are said to be absorbed. When nutrients and oxygen meet these enzymes, they combine to form carbon dioxide, water, and energy. The liberated energy is used to synthesize ATP (adenosine triphosphate). This ATP then diffuses throughout the cell and releases its energy whenever it is needed for cellular functions.

e. **Lysosomes.** Lysosomes (figure 2-2) may be called the digestive organs of the cell. Lysosomes are surrounded by a membrane and contain digestive (hydrolytic) enzymes. When this membrane ruptures, it releases the digestive enzymes that will break down particles or molecules located near the ruptured area. For example, they surround pinocyticle vesicles containing food particles and digest them. If a sufficient number of lysosomes rupture, the entire cell may be digested. When the lysosomes function properly, products of digestion can be used by the cell.

f. **Nucleoli.** In the nucleus of many cells, there may be one or more structures called nucleoli (figure 2-2). The nucleoli do not have a limiting membrane, as do most organelles. These structures are primarily aggregate of loosely bound granules composed mainly of ribonucleic acid (RNA). Hereditary units called genes are thought to synthesize and store in the nucleolus. This stored RNA diffuses into the cytoplasm where it controls cytoplasmic function. Therefore, the main functions of the nucleolus are the synthesis of RNA and the storage of RNA.

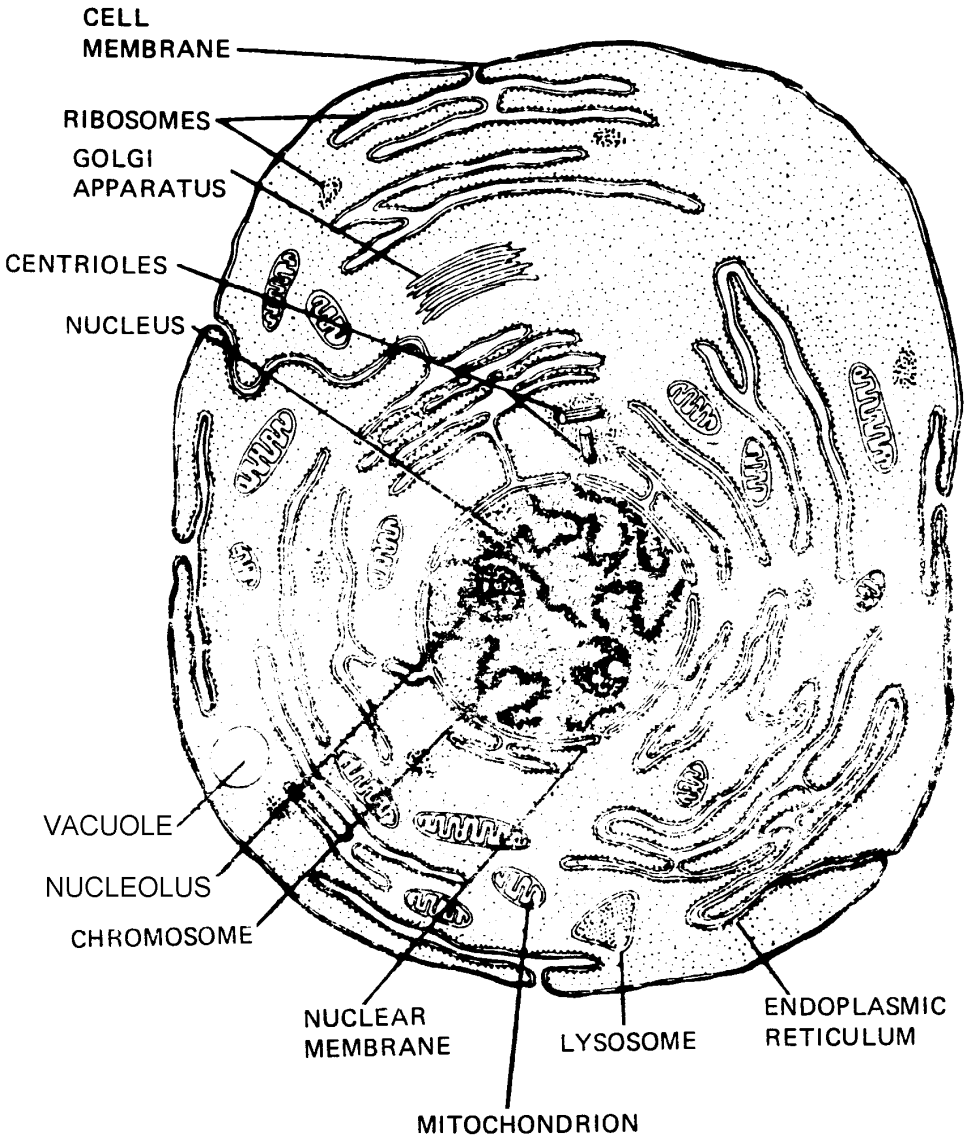


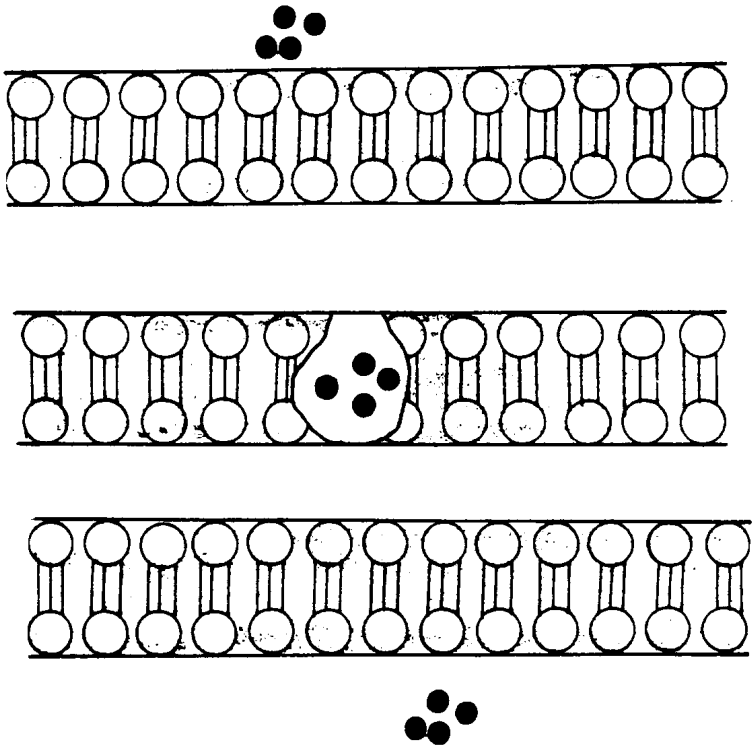
Figure 2-2. Diagram of the cell.

g. **Endoplasmic Reticulum.** The endoplasmic reticulum (figure 2-2) is a network of tubules and vesicles (saclike structures) in the cytoplasm. The inside of the tubules and vesicles is filled with endoplasmic matrix, a fluid medium, which is different from the fluid outside the endoplasmic reticulum. In the matrix, there are enzyme systems. The first function of the endoplasmic reticulum is to use these enzymes to synthesize various substances (that is, lipids). The endoplasmic reticulum is connected to the nuclear membrane and, in some cases, it is connected directly through small openings to the exterior of the cell. A second function of the endoplasmic reticulum is to transport various substances, through the vast network of tubules, from one part of the cell to another area of the cell. A third function of the endoplasmic reticulum is to store various substances within the cell.

h. **Ribosomes.** Ribosomes (figure 2-2) are small particles that are usually attached to the endoplasmic reticulum. Ribosomes are the site of protein synthesis and are referred to as "protein factories" of the cell. Ribosome is composed mainly of ribonucleic acid (RNA).

2-6. PINOCYTOSIS

Pinocytosis is the engulfing of small particles or fluids by the cell. That is, when these substances meet the cell membrane, they cause the membrane to form a channel. At the end of this channel, small vesicles form. These vesicles contain the substance and some extracellular fluid. The vesicle then breaks away from the rest of the membrane and migrates toward the center of the cell. Figure 2-3 illustrates the process of pinocytosis.



1. Particles contact cell membrane.

2. Vesicle (saclike structure) is formed.

3. Vesicle containing the particles passes into the cell.

Figure 2-3. Pinocytosis.

2-7. PHAGOCYTOSIS

Phagocytosis is the engulfing of solid particles by a cell. For example, bacteria could be surrounded and ingested by a cell. The mechanism of phagocytosis is similar to that of pinocytosis. However, in phagocytosis, the cell acts to surround the particle with the cell membrane and form a vesicle (sac) containing the particle and cytoplasm. Then, the vesicle breaks away from the cell wall and moves toward the center of the cell. Figure 2-4 illustrates phagocytosis.

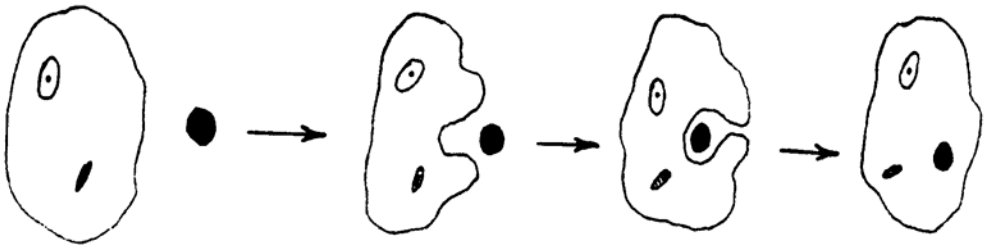


Figure 2-4. Phagocytosis.

Section III. TISSUE

2-8. DEFINITION OF TISSUE

A tissue is composed of a group of cells, which are the same or similar in nature. For example, liver cells are bound together into a tissue called liver, and bone cells are bound together with a large amount of lime salts to form bony tissue. The various tissues of the body have different characteristics because the cells that make up these tissues are different both in structure and in function.

2-9. TYPES OF TISSUE

There are four primary tissues as follows: epithelial, connective, muscular, and nervous.

a. **Epithelial.** Epithelial tissue (figure 2-5) covers the outer surface of the body and forms the lining of the intestinal and respiratory systems. A special form called endothelium lines the heart and blood vessels. As serous membranes, it lines the cavities of the abdomen, the chest, and the heart, and covers the organs that lie in these cavities. Epithelial tissue forms the glands and parts of the sense organs. According to its location, this tissue has different functions. As the skin, it protects underlying structures; in the small intestine, it absorbs; in the lungs, it is a highly permeable membrane; in glands, it secretes; and in the kidneys and liver, it both secretes and excretes. There are three types of epithelial tissue based on the shape of the cells. These are squamous (flat), cuboidal, and columnar. These cells are further designated as simple if they are arranged in a single layer, or stratified if arranged in layers.

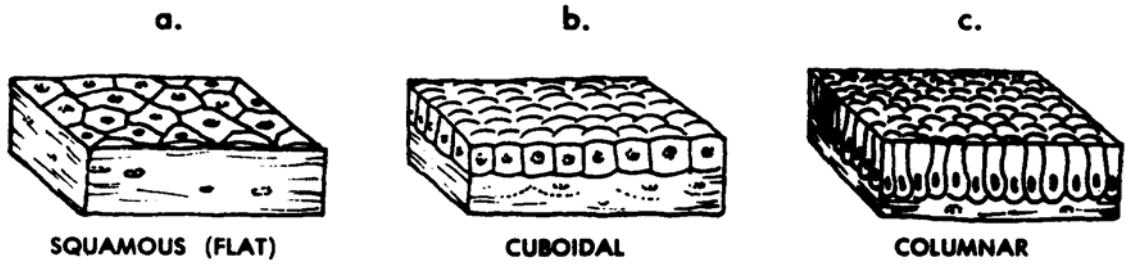


Figure 2-5. Epithelial tissue.

b. **Connective.** Connective tissue (figure 2-6) is widely distributed throughout the body. It binds other tissues together and supports them, forms the framework of the body, and repairs other tissues by replacing dead cells. Principal types of connective tissue are osseous (bony), cartilaginous, fibrous, elastic, and fatty. Areolar tissue, which lies under the skin and serves to fill many of the sharp corners and small spaces of the body, is a mixed type composed of fibrous, elastic, and fatty connective tissue.

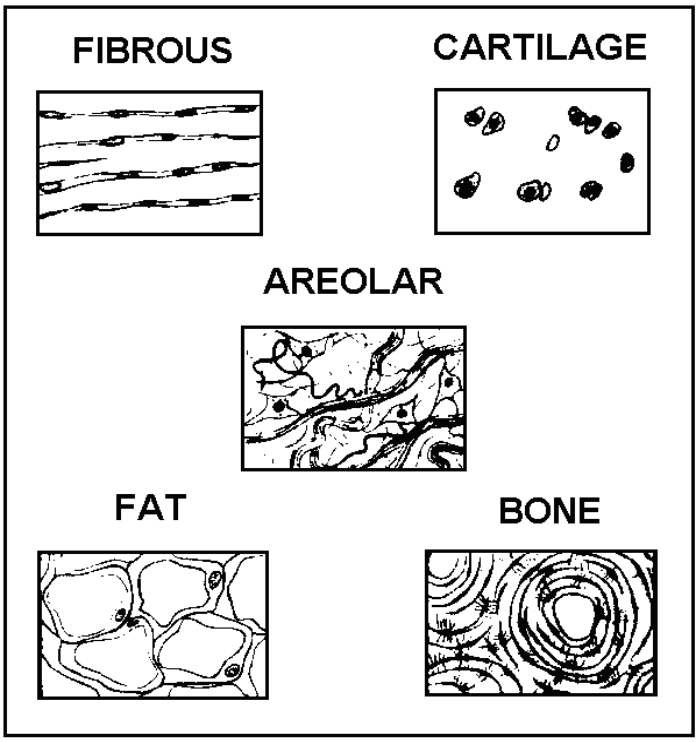


Figure 2-6. Connective tissue.

c. **Muscular.** Muscular tissue (figure 2-7) is of three kinds: voluntary (striated), involuntary (smooth), and cardiac.

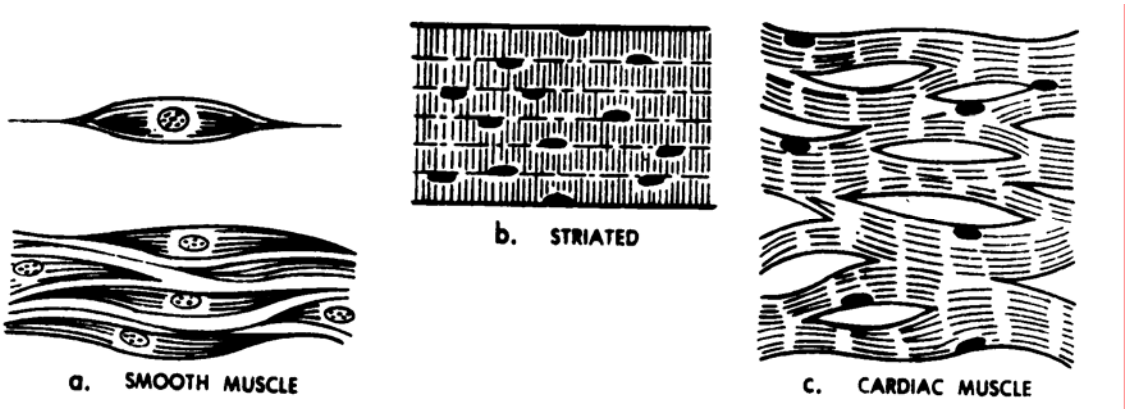


Figure 2-7. Muscle tissue.

d. **Nervous.** Nervous tissue (figure 2-8) is made up of nerve cells (neurons) and supporting structure of nervous tissue (neuroglia).

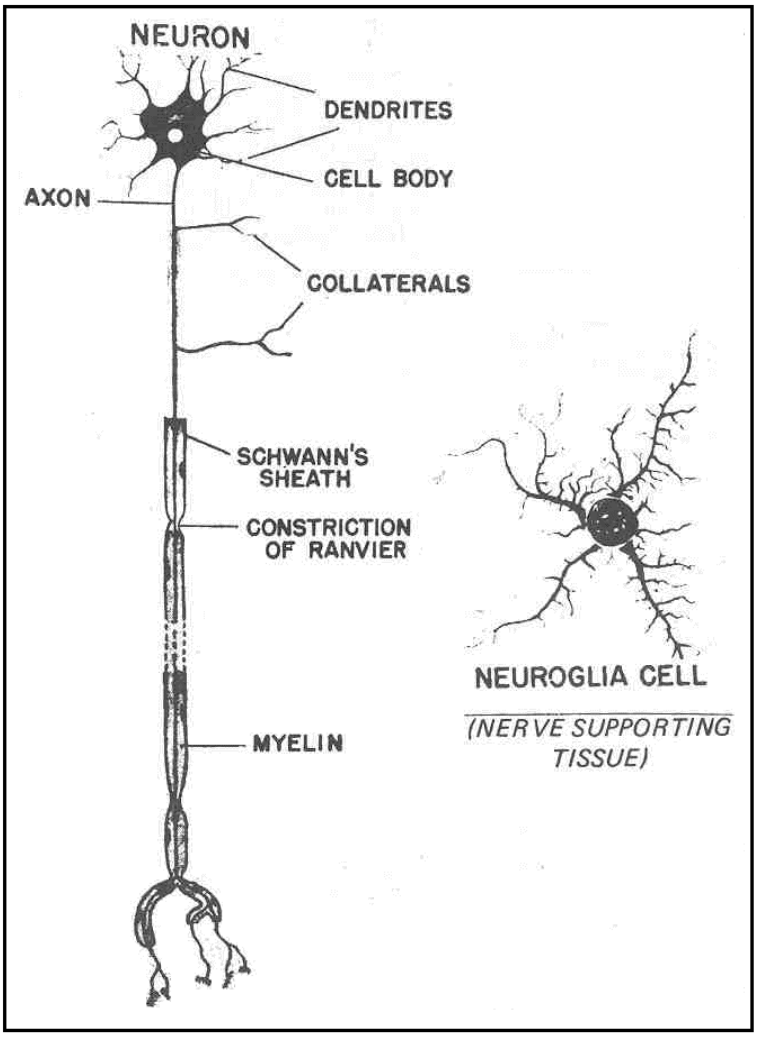


Figure 2-8. Neuron and neuroglia.

Section IV. SKIN

2-10. DESCRIPTION OF SKIN

The skin is a tough, elastic structure covering the entire body (figure 2-9). It is made up of two principal layers, the epidermis or cuticle and the dermis or true skin. The epidermis, which overlies the dermis, is itself composed of a superficial layer and an inner layer. The superficial or horny layer consists of dead cells that are constantly being worn off. These are replaced from the living cells that form the inner layer. The dermis is the thicker part of the skin, and consists of connective tissue containing blood vessels, nerve endings, sweat glands, sebaceous glands, and hair follicles. The dermis is held in place by a layer of areolar connective tissue.

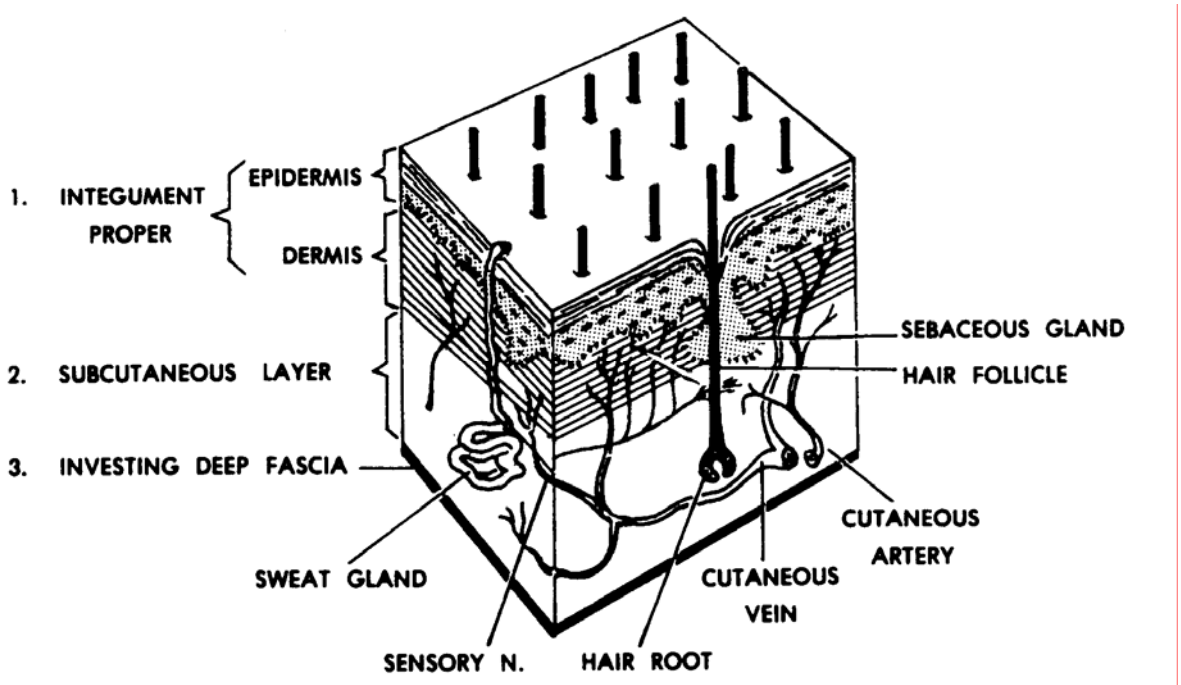


Figure 2-9. Structure of the skin (cross section).

2-11. FUNCTIONS OF THE SKIN

a. **Protection.** The skin protects underlying structures by acting as a mechanical barrier. When the skin is broken, bacteria may invade the body through the opening.

b. **Regulation of Body Temperature**. The skin regulates the body temperature by controlling heat loss in two ways:

(1) The blood vessels in the skin change in size; they dilate and bring warm blood to the surface to increase heat loss, and they constrict to decrease heat loss.

(2) The skin produces sweat which, when it evaporates, cools the body surface.

c. **Sensory Perception**. The skin acts as an organ of perception. It contains sensory nerve endings which are specialized to detect heat, cold) pressure (touch), and pain.

d. **Excretion**. The excretion of waste products through the skin is a function of the sweat glands that open by a duct onto the skin surface. The opening is called a pore. These glands are distributed in large numbers over the body and secrete an average of a quart of perspiration each day; although, the amount varies considerably, depending on the temperature and humidity of the atmosphere, and the amount of exercise performed by the individual. Perspiration is continuous, but it may be so slow and the sweat may evaporate so quickly that it is imperceptible. Sweat consists chiefly of water (99 percent), with small quantities of salts and organic materials which are waste products. Skin also secretes a thick substance, sebum. This material is the product of the sebaceous glands, and its purpose is to lubricate the skin and keep it soft and pliable.

e. **Absorption**. Although not one of its normal functions, the skin is capable of absorbing water and other substances. Physicians take advantage of this fact by prescribing local application of certain drugs.

2-12. APPENDAGES OF THE SKIN

The appendages of the skin include the glands (sweat and sebaceous), the hair, and the nails. Each hair consists of a shaft (the portion projecting from the surface) and a root (the part implanted in the skin); each hair root is implanted in an involution of the epidermis called the hair follicle. A fingernail or toenail grows from a nail bed. If the bed is destroyed, the nail will no longer grow.

2-13. DISEASES OF THE SKIN

a. **General.** Diseases of the skin make up a large portion of the physician's practice, whether in civilian life or in the Army. A specialist in diseases of the skin is called a dermatologist. Descriptive terms used in dermatology are:

(1) Bulla--large blister filled with serous fluid.

(2) Excoriation--superficial discontinuity or scratch.

(3) Induration--hardness.

(4) Lesion--any localized abnormality.

(5) Macula--small, flat discoloration or freckle.

(6) Papule--small, elevated lesion.

(7) Pruritis--intense itching.

(8) Pustule--vesicle containing pus.

(9) Squamous--scaly.

(10) Vesicle--small blister.

b. **Virus Infections**. Virus infections of the skin include the follows:

(1) Verruca vulparis. Verruca vulparis is the common wart.

(2) Herpes simplex. This is often called a fever blister, or cold sore.

(3) Herpes zoster. Herpes zoster is a painful infection commonly known as shingles.

c. **Bacterial Infections**. Bacterial infections of the skin include the following:

(1) Furuncle (also called "boil.") This is an acute, inflammatory lesion produced by the infection of a hair follicle or a skin gland by staphylococci bacteria. The lesion begins as a pustule. As the pustule enlarges, the skin becomes reddened, tense, and shiny. Pain and tenderness develop. The furuncle rapidly matures (comes to a head), and usually ruptures spontaneously, discharging pus. The treatment is heat, and incision and drainage. Under certain circumstances, antibiotics, such as penicillin, are indicated.

(2) Carbuncle. A lesion that resembles the furuncle, since it has the same cause and early course, but carbuncles are larger, and produce fever and leukocytosis (elevated white cell count in the blood). When a carbuncle ruptures, pus is discharged through several openings in the skin. The treatment consists of surgical drainage of the carbuncle and penicillin.

(3) Cellulitis. An acute, deep-spreading inflammation of the skin and subcutaneous tissues. Streptococcic infections tend to spread more than staphylococcic infections, because they produce an enzyme which breaks down the wall the body tries to form around the infection. The skin becomes red, tender, and swollen. The patient has fever. The infection may spread through lymph vessels, producing red streaks on the skin. It may enter the bloodstream and be carried through the body (septicemia or blood poisoning).

d. **Fungal Infections.** Fungal infections are among the most common of all diseases. In order for the fungi to produce skin infection, certain favorable conditions are required. Some of these conditions are: lack of cleanliness; excessive moisture, usually due to perspiration; and irritation of the skin, usually because of tight clothing.

(1) Dermatophytosis pedis. Dermatophytosis pedis (also called tinea pedis and athlete's foot) may be recognized by the presence of superficial fissures between and toes, and vesicles on the sides and beneath under the toes. If secondary bacterial infection occurs, pustules appear, and ulceration may result.

(2) Dermatophytosis (tinea) corporis, capitis, and cruris. These fungous infections are commonly called ringworm. Dermatophytosis (or tinea) cruris is also called "jock itch." The diagnosis of ringworm is made by the presence of a few (usually not over two or three) circular, ring-like, red, scaling lesions, clearing at the center, with advancing vesicular margins. Tinea cruris is distinguished by its location on the upper surface of the thighs. Excessive perspiration and friction from clothing are important contributing factors. Therefore, an important part of the treatment consists of exposing the involved parts to the air as much as possible.

e. **Arthropod Infestations and Infections.** The arthropods are many-celled animals with outer skeletons but without backbones, and include such organisms as crayfish, spiders, mites, ticks, centipedes, and insects (lice, mosquitoes).

(1) Pediculosis. Pediculosis is an infestation of the skin with lice.

(a) Diagnosis of louse infestation. Lice have a habit of living in the clothes and bedding of patients and coming out only at the night to feed. This fact must be taken into account when examining a patient suspected of being infested. The small louse bites may be quite difficult to locate in the absence of the louse, although the patient has usually scratched the skin in the area very vigorously, leaving scratch marks.

(b) Treatment. Pediculosis is treated by application of gamma benzene hexachloride (Lindane®).

(2) Scabies. Scabies is a disease caused by a very small mite that burrows into the skin. The infection often begins between the fingers, and spreads to the body, especially the lower abdomen, buttocks, and genitalia. The mite causes much itching (especially at night), and there is abrasion of the skin from scratching. Secondary infection by bacteria may occur, with the formation of pustules. The abrasions and pustules often obscure the typical lesions of scabies, which are threadlike, twisted lesions with a small raised area at one end. All washable clothing should be thoroughly laundered, and other clothing dry-cleaned.

f. **Allergic Conditions**. In allergic conditions, the patient is sensitive to certain foreign substances that may contact his skin, or be introduced into his body in the food he eats or the air he breathes. A first contact is necessary to produce the sensitization, following which the patient reacts to contact with the foreign substances in an abnormal manner. Some substances can provoke an allergic reaction in anyone contacting them. Others appear to produce allergy only in certain individuals who have a constitutional or inherited predisposition to allergy.

(1) Urticaria. Urticaria (commonly called hives) is an allergic condition which results in the formation of wheals (rounded or irregular shaped, transitory elevations of the skin). Urticaria is usually caused by eating a substance to which the patient has been sensitized, but may also be caused by a local allergen such as poison ivy; or it might have a psychogenic origin. It is usually associated with much itching and may cover the whole body. Often it is difficult to determine the cause, and the disease may constantly reoccur.

(2) Contact dermatitis. Contact dermatitis (dermatitis venenata) is due to sensitization of the skin by direct contact with a sensitizing substance. The development depends on how much of the substance is contacted, and how often. Why sensitivity occurs is not known. At the beginning, the skin is reddened in the contacted area, then raised lesions appear, and then blisters. The lesions may spread over the body. The vesicles may become infected by bacteria, and pustules appear. There is marked itching. The patient may carry the sensitizing substance to other skin areas by his hands. The sensitizing substance may be almost anything. Examples include: poison ivy, medicines, clothes, and soaps. A painstaking and thorough search is necessary to find and remove the allergen. Treatment includes removal of the allergen, mild bland applications, and antihistaminics in some cases.

g. **Other Conditions**.

(1) Psoriasis. Psoriasis is a chronic, recurrent disease of the skin, characterized by reddish, rounded lesions that are covered by silvery scales. When a scale is removed, it leaves a small bleeding point. The disease tends to begin on the elbows, knees, or scalp, and to spread over the whole body.

(2) Acne vulgaris. Acne vulgaris is a chronic inflammation of the sebaceous glands (oil glands) of the skin, which usually develops during adolescence. Lesions develop rapidly and in crops, located mostly on the face, sometimes on the sternal region, the shoulders, and the back. The lesions may cause considerable scarring on healing. Treatment includes good personal hygiene to help prevent secondary infections, dietary measures, antibiotics, and various skin lotions.

2-14. SIGNS AND SYMPTOMS OF SKIN DISEASE

a. **Pruritis (Itching).** The most common, most annoying, and least specific symptom encountered in dermatologic conditions is pruritis. Among the causes of itching may be included infectious agents, allergic conditions, neuroses, parasitic infestations, dryness of the skin, anoxia of the skin, and chronic irritation of the skin. The actual pathological change responsible for this symptom takes place in minute nerve endings in the skin. The exact change is not known, but these endings become increasingly sensitive to the various causative agents, and itching will appear more easily.

b. **Pain**. Pain is not seen very often in skin disorders, although there may be a burning sensation associated with indurating lesions.

c. **Edema.** Edema is the collection of fluid in the tissues of the dermis. This is usually localized at least to a particular area of the body. When individual lesions take the form of a small area of swelling with associated pruritis, the eruption is called urticaria. The edema may be extensive, involving either the face or part of an extremity. When the edema involves the face, the eyes may be forced shut by the swollen tissues. Edema is seen in numerous systemic disorders, but there are usually enough other symptoms of the underlying disease to prevent confusion with a skin reaction to an allergen.

d. **Scales**. The upper layer of the epidermis may accelerate the production of keratinized (horny) cells, and these will begin to flake off following minimal trauma. These flakes of dry, dead tissue are called scales. Many lesions show scaling as the disease kills additional layers of the epidermis. Occasionally the scales may take characteristic shapes because of plugging pores in the skin.

e. **Weeping**. Weeping is the oozing of fluid from the surface of a lesion. This occurs whenever sufficient layers of epidermis have been destroyed and removed so that the capillary beds of the dermis are near the surface. Weeping is serious because of its tendency to macerate (soften) the lesions and the surrounding skin. As the healthy tissue breaks down, the disease spreads more easily. Weeping is frequently seen in body creases and must be guarded against. The use of powders to dry weeping lesions is the first step in the successful therapy of such conditions.

f. **Scaling and Weeping**. There may be a combination of scaling and weeping. This will result in the formation of a crust over the lesion. Any blood, pus, or other exudate from the lesion may add to this crust. The raw surface of the lesion will be protected by this crust, but the fluid collecting under it will be an excellent growth medium for bacteria, thus adding infection to the existing problems. Crusts may be a cause of itching, and frequently they will be ripped off by the patient, either on purpose or accidentally while scratching.

g. **Fissures**. Fissures are small cracks in the skin. These are very common and occur when there is an excessive drying of the skin. The corners of the mouth are common sites for this condition. Fissure may also be seen in areas of lichenification (places where the tissue has become thickened from continuous irritation). Fissures are open portals of entry for bacteria.

h. **Fever**. Fever is usually seen in infectious diseases, but it may also be present in cases of allergy. This is not a common concern to the dermatologist, because disease limited to the skin will not cause fever.

2-15. TREATMENT

a. **Symptomatic**. Many forms of treatment are available for disorders of the skin. Frequently, treatment is instituted merely to relieve the distressing symptoms and may have no effect on the course of the disease. The antipruritic (anti-itch) medications are of this type. Both lotions and powders are used and are effective in a fair percentage of cases. Systemic antipruritics are not very effective but are of some use in systemic diseases that have itching at some stage. Antihistamines are used primarily in allergic reactions, and they are extremely effective in relieving the itching as well as in suppressing the skin lesions.

b. **Drugs**.

(1) Antibiotics. Antibiotics may be used topically when there is an infection in the skin, either primary or secondary. The infection should always be present before the antibiotic is used. The prophylactic (preventive) use of topical antibiotics is dangerous because these drugs have a higher than usual incidence of sensitivity reactions when used in this manner.

(2) Steroids. The numerous synthetic steroid preparations have been of great assistance to the dermatologist. Many diseases will be controlled by steroids after all other means of treatment have failed. Steroids usually are given systemically, and they may cause serious consequences; therefore, steroids are normally used only after other means of therapy have failed. The topical use of steroids, however, is effective and safe because negligible quantities are absorbed, even through raw lesions.

(3) Antipyretics. Aspirin and acetaminophen are the most effective agents available for reducing temperatures.

Section V. NATURE AND CAUSES OF DISEASE

2-16. DEFINITION OF DISEASE

Disease can be defined as a derangement of the normal functioning of one or more of the body processes. This interference with the normal body functions either prevents them from taking place, or causes them to act in an abnormal manner. For example, a tumor may obstruct the flow of intestinal contents, or bacteria may cause irritation or inflammation. In the following text, consideration will be given to those factors which are responsible for interference with the normal body functions, in other words, the etiology (causes) of disease.

2-17. CAUSES OF DISEASE

There are nine major causes of disease (a through i below). Frequently a disease may be produced by a combination of these causes, or the same disease may be caused by different factors in different patients, or the cause may be unknown (see paragraph j below).

a. **Prenatal Influences**. By this is meant those factors which may operate before birth to produce disease in the offspring; factors may be manifested at birth (congenital disease) or may not become obvious until later in life.

(1) Heredity. Among prenatal factors, one influence is heredity. A disease may be genetically transmitted from a parent to offspring. The parents who transmit the disease to their offspring may or may not have the disease themselves. Examples of some hereditary diseases are hemophilia and congenital dislocation of the hip.

(2) Congenital influence. Diseases affecting the mother while she is pregnant with the baby may adversely affect the offspring. For example, some diseases may be transmitted directly to the baby via the bloodstream, as is often seen in the case of syphilis in the mother. Alternatively, the pregnant woman may have a disease such as German measles, which interferes with the normal development of the child in the uterus (in utero), although, the child does not acquire the disease. Malnutrition in the mother could result in a poorly nourished baby, which could also interfere with the normal development of the child.

(3) Mechanical. Purely mechanical factors are also felt to be responsible for some abnormalities present at birth. Abnormal positioning of the baby in utero is felt to be occasionally responsible for wryneck; torsion or twisting of the umbilical cord would limit the blood and food supply to the baby, and dire results could occur. Any defect or disease present at the time of birth is called a congenital disease or condition. Injuries or effects sustained during the process of being born may be included here.

b. **Parasites**. Parasites are organisms that live on or within the body of the man or any other living organism, and at the expense of the one parasitized. Parasites may live on the surface of the skin (ectoparasites), or they may enter the body through the skin, the respiratory tract, the gastrointestinal tract, or the genitourinary tract where they may enter the bloodstream and be carried to distant parts of the body. If they live inside the body, but outside the cells, they are called extracellular endoparasites; if they enter the body's cells, they are called intracellular endoparasites. They all cause disease by interfering with the tissue and organ functions; they accomplish this by elaborating toxins, or poisons; by causing inflammation, or irritation; by producing enzymes which destroy tissue; and by causing mechanical blockage of function.

(1) Viruses. These are the smallest agents known to produce disease; whether they are living organisms or complex chemical compounds is not known. They are known to be intracellular endoparasites that cause such common diseases in man as poliomyelitis, common cold, influenza, measles, mumps, chickenpox, smallpox, hepatitis, encephalitis, warts, rabies, yellow fever, and lymphogranuloma venereum.

(2) Rickettsiae. These organisms are larger than viruses, but are still very small intracellular endoparasites. These organisms are transmitted to man by mites, ticks, fleas or lice, and they produce Rocky Mountain spotted fever, typhus (epidemic and endemic), scrub typhus (tsutsugamushi fever), Q fever, and Rickettsialpox.

(3) Bacteria. Bacteria are minute, one-celled, organisms that may occur alone or in large groups called colonies. Significant bacteria can be divided by their shape into three main groups.

(a) Cocci. Cocci are round, one-celled bacteria. The primary members of this group are staphylococci, which group themselves in clusters; streptococci, which arrange themselves in chains; and diplococci, which arrange themselves in pairs. All are pyogenic (produce pus).

(b) Bacilli. Bacilli are rod-shaped; however, they vary from straight to irregular-curved and branched shapes. They cause such common diseases as typhoid fever, diphtheria, tuberculosis, and leprosy.

(c) Spirochetes. Spirochetes are spiral-shaped and can move or twist. Spirilla and Treponema pallidum are examples. The latter causes syphilis.

(4) Fungi. These extracellular endoparasites or ectoparasites are larger and higher in the scale of plant life than are the bacteria. They include the yeast and molds, and produce infections of the skin such as ringworm, and infections of the mucous membranes such as thrush. Some attack internal organs, especially the lungs and central nervous system, very often with disastrous results.

(5) Protozoa. These are one-celled animal parasites (either extracellular or intracellular) that cause such common diseases as malaria and amoebic dysentery.

(6) Metazoa. These many-celled, larger animals include the helminthes (worms) such as the ascaris, the hookworm, the pinworm, the tapeworms, and the flukes, as well as the arthropods (mites, lice, and so forth.).

c. **Intoxicants.** Intoxication is the process of taking any chemical substance that causes disease or injury into the body. Many substances are very useful in small amounts, and do not cause intoxication; but the same substances may be very toxic in larger amounts, and result in severe illness or death.

d. **Trauma.** Trauma may be defined as injury sustained by the body as the result of a physical agent or force. The physical agents that may produce trauma or injury of the body are:

(1) Light. In excessive amounts, light can cause temporary blindness.

(2) Heat. Excessive heat can cause burns of the body, heat cramps, heat exhaustion, or heatstroke.

(3) Cold. Cold is absence or deficiency of heat. Exposure to low temperatures can result in frostbite and other cold injury.

(4) Electricity. One can sustain burns, electric shock, or both when exposed to this agent.

(5) Ionizing radiation. Excessive exposure to x-rays or to radioactive elements can produce burns, radiation sickness, malignancies, cataracts of the eye, and genetic changes.

(6) Mechanical forces. These agents produce contusions, abrasions, lacerations, fractures, sprains, and strains.

(7) Sound. Exposure to excessive noise can cause temporary or permanent deafness to certain wavelengths.

e. **Circulatory Disturbances.** Any interference with the blood flow to a portion of the body results in a circulatory disturbance.

(1) Ischemia. A decrease in the normal diameter of an artery supplying a portion of the body results in a decrease in the amount of blood that flows to the part. The area becomes more pale and colder than normal, and is said to be ischemic.

(2) Thrombosis. Whenever a vessel wall becomes diseased, the blood tends to collect at the diseased or injured site and form a thrombus (clot). The presence of an intravascular blood clot is called thrombosis.

(3) Embolism. Portions of a thrombus may break loose, and then travel freely in the bloodstream until stopped by a vessel too small for the particle to pass through; or foreign particles, such as air bubbles or fat globules, may be introduced into the bloodstream and travel freely until stopped by a smaller vessel. These foreign particles are known as emboli. The process of obstruction or occlusion of a blood vessel by a transported foreign material is known as embolism.

(4) Gangrene. When an extremity or portion thereof loses its arterial blood supply as the result of thrombosis, embolism, trauma, or from any other cause, a massive area of the tissue dies, and is said to have undergone gangrene, or to have become gangrenous.

(5) Infarction. Death of the tissue of an organ or portion thereof as the result of the loss of its blood supply is known as infarction. The necrotic (dead) area itself is called an infarct.

(6) Hemorrhage. This is the loss of blood.

f. **Neuropsychiatric Disturbances**.

(1) Organic disorders. Injury or disease of the nervous system tissue may result in the loss of the nerve supply to a particular part of the body. Therefore, because of loss of enervation, secondary changes in the tissue occur, such as atrophy. In addition, the normal functions may become paralyzed, and there may be loss of sensation and other changes.

(2) Functional disorders. Disturbances of the mind or psyche may produce neuroses, psychoses, or character and behavior disorders. Such disturbances may or may not be inherited; the environment, childhood experiences, and many other factors have a bearing on the production of psychiatric disturbances.

g. **Mechanical Disturbances**. Certain static mechanical abnormalities may result in disease within the body. For example, volvulus or twisting of the intestine on itself, torsion of the spermatic cord, strangulation of a hernia, and intussusception, are all often on a purely mechanical basis.

h. **Disorders of Metabolism, Growth, or Nutrition**. Metabolism has to do with the total chemical cycle of converting substances into forms that are usable to the body. Metabolism occurs in two phases.

(1) Anabolism. In anabolism, foodstuffs are broke down (digested) and reconverted into compounds which can be utilized as energy, or as building blocks for new tissue cells and substances. In anabolism, living tissue is manufactured from nonliving substances. This results in growth or replenishment.

(2) Catabolism. Catabolism is the breaking down of the body's complex substances by wear, tear, and age into waste products of simpler composition for elimination. Metabolism and growth then are dependent on the body's receiving enough of the proper foodstuffs in order to supply its needs, in other words, on proper nutrition. Metabolism and growth are further regulated by the vitamins and hormones. The hormones are supplied by the ductless glands of the body (the pituitary, thyroid, parathyroid, pancreas, adrenals, and gonads), and any disorder of these glands will profoundly disturb growth and metabolism. The vitamins are supplied by the diet; if the diet or nutrition is unsatisfactory, disturbances in growth and metabolism can result also. Therefore, metabolism, growth, and nutrition are closely related to one another.

i. **Neoplasms**. Normally, the body grows by multiplication of its cells. At first, in the embryo, these cells are all alike or undifferentiated. However, as they multiply, they come under the influence of certain factors and take on different forms and different functions to make up the different tissues, organs, and systems of the body (that is, they become differentiated). This growth and differentiation is a slow, methodical, controlled process. However, some cells may not differentiate entirely, but for some unknown reasons, retain varying degrees of undifferentiation, break free of their growth control, and form a new growth (neoplasm) or tumor. Tumors cause disease by interfering with the function of normal cells, tissues, and organs. They may cause pressure on an organ so that its normal cells are destroyed or its blood supply is shut off. A tumor may fill the cavity of an organ so that the organ wall cannot contract properly. The tumor may also use up the nutritive materials taken into the body so that there is not enough for the normal tissues. Tumors are of two types: benign and malignant.

(1) Benign. These are more slowly growing, the cells are more differentiated, the tumor is well separated from the surrounding tissues by its capsule, and can usually be completely removed surgically.

(2) Malignant. These are more rapidly growing with very little growth control, and the cells are more primitive or undifferentiated. The cells of the tumor infiltrate or grow between the normal tissue cells, and are much more difficult to remove surgically. Because of this, the malignant tumor tends to recur and tends to metastasize or spread via the blood and the lymph vessels. The common term for malignant tumors is cancer. The medical profession speaks of carcinoma when the malignant tumor arises from tissue that covers the surface of the body, lines a hollow structure, or forms glands, and sarcoma when the malignant tumor arises from any other tissue in the body such as fatty, muscular, bony, or fibrous tissue.

j. **Idiopathic (Unknown) Causes**. There are many diseases of known etiology. The affected organ and effective treatment are often known, however, the cause and the mechanism through which the disease disrupts the body's functions remain unknown.

Section VI. TREATMENT OF DISEASE AND INJURY

2-18. INTRODUCTION

Patients who have disease or injury must be properly diagnosed and treated. The physician is responsible for these functions; however, the physician may delegate the accomplishment of some of the treatments to other members of the Army Medical Department (that is, physicians' assistants and physical therapists). In general, all types of treatment may be classified as either preventive or corrective.

2-19. PREVENTIVE TREATMENT

Preventive treatment includes all measures used to prevent disease.

a. Preventive procedures include sanitary measures such as cleanliness, proper waste disposal, inspection of food and food handlers, isolation diseased individuals, aseptic surgical technique, and the use insecticides of and rodenticides to control vectors of disease.

b. Another preventive measure is immunization. Active immunity is the result of a direct introduction into the individual's body of an antigenic preparation (frequently bacteria or viruses) so that an individual produces his own antibodies that defend him against the particular antigen introduced. Passive immunity is produced by injecting serum-containing antibodies into an individual. This blood serum may be from animals or humans in which the antibodies were produced by an active immunity process.

c. A third preventive measure consists of preventive psychiatry and mental health work, in which the individual or his environment is manipulated in a manner to prevent excessive mental stress.

2-20. CORRECTIVE / SYMPTOMATIC TREATMENT

People who have some disease or condition want to receive prompt medical treatment. Many people believe that the use of prescribed medications is the only way to ensure that a disease or condition will be cured or improved. The use of drugs does have an important role in the treatment of disease; however, other treatment methods are available. For example, rest, radiotherapy, and physical therapy are very useful in the treatment of certain conditions. In many cases, various treatment methods are used to benefit the patient.

a. Rest prevents overwork of a diseased organ and includes more than freedom from physical work; a patient must have mental rest also.

b. Diet is of extreme importance both in the prevention of disease and in medical care. An adequate intake of proteins, carbohydrates, fats, vitamins, and minerals is necessary in the treatment of all patients. Patients with fever generally require increased amounts of all dietary constituents. Patients with certain diseases require diets in which the various dietary constituents are carefully controlled. One example of a special diet of this type is that for diabetes mellitus, in which the amounts of protein, fat, and carbohydrates must be individually regulated.

c. Nursing care is another essential part of medical care. In addition to doing technical procedures such as administering drugs, nursing service personnel watch for the appearance of changes in the patient's condition. Frequently the personalities of such personnel will be an important factor in promoting the patient's morale, securing his cooperation, and fostering in him a desire to get well.

d. Drugs are substances used in the treatment of disease. They are used to relieve the unpleasant effects of disease and to eradicate the disease. Drugs may be administered externally and internally.

e. Radiotherapy is the use of x-rays, radium, and radioactive isotopes in the treatment of disease.

f. Occupational therapy is treatment that provides a patient with activity to keep his mind and body occupied. It is also used to help the patient regain muscular coordination and control of specific parts of the body.

g. Physical therapy is the treatment of disease by physical means. Various agents used in physical therapy are light, heat, cold, electricity, water, massage, and exercise.

h. Psychotherapy is treatment by various means, which may include the use of drugs, to lessen or rectify abnormal mental conditions. Surgery performed for the same purpose is called psychosurgery.

i. Surgery is the treatment of disease by manual operation or corrective apparatus. It includes the removal of diseased tissue or organs and the repair of injured structures.

Continue with Exercises

EXERCISES, LESSON 2

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the definition below, select the definition of the term anatomy.

   a. The study of the functions of the body.

   b. The study of the chemical substances in the body.

   c. The study of the structures of the body.

   d. The study of the systems of the body.

2. From the definitions below, select the definition of the term tissue.

   a. A grouping of like cells working together.

   b. The smallest living unit of body construction.

   c. A group of organs working together.

   d. A group of cells that have nothing in common.

3. From the functions below, select the function of the lymphatic system.

   a. Protects the body from drying.

   b. Returns proteins and fluid from the various body tissues to the blood.

   c. Manufactures hormones.

   d. Provides nutrients to the various limbs of the body.

4. From the descriptions below, select the best description of the cytoplasm.

    a. Organelles that perform highly specialized functions in the cell.

    b. A jelly-like substance that coats the outside of the cell membrane.

    c. The part of the cell which manufactures RNA and DNA.

    d. The fluid or semifluid contained inside the cell membrane, but outside the nucleus.

5. From the descriptions below, select the best description of the mitochondria.

    a. The organelle of the cell responsible for producing DNA.

    b. The site of cell respiratory activity.

    c. The part of the cell which is responsible for producing RNA.

    d. The organelle responsible for monitoring the flow of water into the cell.

6. From the definitions below, select the definition of pinocytosis.

    a. A vesicle which engulfs and destroys the cell.

    b. The organelle responsible for producing extracellular fluid.

    c. The production of fluids by the cell.

    d. The engulfing of small particles or fluids by the cell.

7. From the descriptions below, select the description of connective tissue.

    a. The tissue that binds other tissues together and supports other tissues.

    b. The tissue that covers the outer layer of the body.

    c. The tissue that forms the glands and the sense organs of the body.

    d. The tissue that covers the organs in the abdomen.

8. From the list of function below, select the function of the skin.

    a. Controls the size of the patient.

    b. Produces chemicals for body growth.

    c. Prevents perspiration on hot days.

    d. Detects heat, cold, pressure, and pain.

9. Select, from the group of descriptions below, the best description of pediculosis.

    a. An infestation of the skin with fungus.

    b. An infection of the skin with bacteria.

    c. An infestation of the skin with lice.

    d. An infection of the skin with ringworm.

10. Select, from the group of descriptions below, the best description of scabies.

    a. A disease caused by a very small mite, which burrows into the skin.

    b. A disease caused by small bacteria, which includes the skin.

    c. A disease characterized by itching and fungal growth.

    d. A disease characterized by the growth of bacteria on the skin.

11. Select, from the descriptions below, the best description of a furuncle.

    a. An acute inflammatory lesion produced by the infection of a hair follicle or skin gland by streptococci bacteria.

    b. An acute, inflammatory lesion produced by the infection of a hair follicle or skin gland by staphylococci bacteria.

    c. An acute lesion produced by an infection of a hair follicle by fungal organisms.

    d. An acute, inflammatory lesion produced by the infection of a hair follicle by allergens.

12. Select, from the definitions below, the meaning of the term pruritis.

    a. A chronic, recurrent disease characterized by reddish, rounded lesions.

    b. A chronic inflammation of the sebaceous glands of the skin.

    c. A parasitic infestation of the skin caused by lice.

    d. Itching.

13. Select, from the descriptions below, a description of edema.

    a. A collection of fluid in the tissues, resulting in swelling.

    b. A raised area of the skin characterized by cellulitis.

    c. A collection of protein in injured tissues resulting in bleeding.

    d. A collection of raised swellings on the skin characterized by itching and discoloration.

14. From the definitions below, select the definition of the term disease.

    a. A condition characterized by functioning of certain glands.

    b. A derangement of the normal functioning of one or more body processes.

    c. A dysfunction of the body caused by lack of exercise.

    d. A dysfunction of the systems of the body characterized by lowered blood sugar.

15. Select, from the descriptions below, the description of physical therapy.

    a. The use of drugs to treat disease of mental origin.

    b. The treatment of disease by the administration of antibodies.

    c. The treatment of disease by such methods of heat, light, and cold.

    d. The treatment of disease by the removal of diseased organs or tissues.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 2

1. c (para 2-1)
2. a (para 2-2b)
3. b (para 2-3f)
4. d (para 2-5b)
5. b (para 2-5d)
6. d (para 2-6)
7. a (para 2-9b)
8. d (para 2-11c)
9. c An infestation of the skin with lice. (para 2-13e(1))
10. a (para 2-13e(2))
11. b (para 2-13c(1))
12. d (para 2-14a)
13. a (para 2-14c)
14. b (para 2-16)
15. c (para 2-20g)

End of Lesson 2

LESSON ASSIGNMENT

LESSON 3	Introduction to Pharmacology.
TEXT ASSIGNMENT	Paragraphs 3-1--3-15.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

3-1. Given a pharmacological term and several definitions, select the definition of that term.

3-2. Given a source of drugs and a list of names of drugs, select the drug that is derived from that source of drugs.

3-3. From a group of statements, select the use(s) of drugs.

3-4. Given a factor that influences drug dosage and a group of statements, select the statement that best describes how that factor influences drug dosage.

3-5. Given a particular route of administration and several statements, select the statement that best describes that route of administration.

3-6. Given a type of adverse reaction to a drug and several statements, select the statement that best describes that type of adverse reaction.

3-7. Given a factor that influences drug action and a group of statements, select the statement that best describes how that factor influences drug action.

3-8. Given one of the following factors that influence drug absorption: water solubility, fat solubility, and transport mechanisms, and several statements, select the statement that best describes how that factor influences drug absorption.

3-9. From a group of statements, select the statement that best contrasts passive transport with active transport.

3-10. Given a group of statements, select the statement that best describes the Receptor Site Theory of the mechanism of drug action.

3-11. Given a group of statements, select the statement that best contrasts competitive antagonists with physiological antagonists.

3-12. From a group of statements, select the statement that best describes the importance of structure activity relationships.

SUGGESTIONS

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 3

INTRODUCTION TO PHARMACOLOGY

Section I. TERMS AND DEFINITIONS IMPORTANT IN PHARMOCOLOGY

3-1. GENERAL

a. It is important for you to be familiar with some terms and definitions frequently used in the study of drugs. Although the terms and definitions presented here are basic, they will provide you with a sound background for gaining additional knowledge, and understanding as you read the text of this subcourse.

b. The terms and definitions provided in this section do not include all the medical terms used in this subcourse. Whenever possible, the meaning of a fairly difficult and unfamiliar term will be written in parentheses ( ) after that term. In the event you encounter a term you do not understand, you should use a quality medical dictionary (such as Dorland's Illustrated Medical Dictionary) to learn the meaning of that term.

c. No attempt is made in this subcourse to address the pronunciation of terms and drug names. If you desire assistance in this area, you should seek the services of someone who works with drugs on a frequent basis. "Pharmacists, pharmacy technicians, nurses, physicians, and other medical personnel are well-qualified to help you to learn the pronunciation of drug names."

3-2. TERMS AND DEFINITIONS

a. **Drug**. A drug may be broadly defined as any substance or group of substances, which affects living tissue. However, the term may be specifically defined as any substance used to prevent, diagnose, or treat disease or to prevent pregnancy.

b. **Pharmacology.** Pharmacology is the study of the actions and effects of drugs on living systems and their therapeutic uses.

c. **Bioavailability**. Bioavailability refers to the amount of drug that is available to the target tissue after the drug has been administered. In other words, it is the amount of the drug available to produce the desired effect.

d. **Pharmacognosy.** Pharmacognosy is the study of the characteristics of natural drugs.

e. **Toxicology**. Toxicology is the science of poisons. Toxicology includes the origin, chemical properties, toxic actions, detection, and proper antidotal therapy of poisons.

f. **Posology**. Posology is the science of dosage. It deals with the amount of drug necessary to produce a desired physiological, therapeutic, or prophylactic effect.

(1) Usual recommended dose. The usual recommended dose is the amount of drug that will ordinarily produce the effect for which the drug is intended. In addition to the usual recommended dose, the usual dosage range is indicated for many drugs in the United States pharmacopoeia/National Formulary. The usual dose range provides a guide in deciding whether the prescriber should be consulted about the correctness of the prescribed dose.

(2) Minimum dose. The minimum dose is considered the smallest dose of drug that produces the therapeutic effect.

(3) Maximum dose. The maximum dose is considered the largest dose of a drug that can be safely administered.

(4) Toxic dose. The toxic dose of a drug is considered the amount of a drug that will produce noxious (harmful) effects.

(5) Lethal dose. The lethal dose of a drug is the amount of substance that will cause death. You will often see the term "LD50" in association with lethal dose. LD50 means that 5O percent (or 1/2) of the animals given that amount of drug died. The LD50 of a drug should be used as a guide, rather than an absolute number.

(6) Single dose. The single dose of a drug is the amount of that substance to be taken at one time.

(7) Daily dose. The daily dose of a drug is the amount of that substance to be taken in a 24-hour period. The daily dose of a drug is into several individual doses.

(8) Maintenance dose. The maintenance dose of a drug is the amount of that substance taken to maintain or continue a desired therapeutic effect. Some drugs must be taken on a daily basis in order to maintain the desired therapeutic effect. For example, drugs used to treat high blood pressure often must be take daily to maintain a lowered blood pressure.

(9) Loading dose. The first dose given of a drug to achieve maintenance drug levels quickly. Drugs that are given only one or two times a day may take two or three days to reach a maximum effect. To overcome this time, a loading dose is given to achieve the levels associated with the maximum effect more quickly. Loading doses are often used in very sick patients.

Section II. INTRODUCTION TO DRUGS

3-3. SOURCES OF DRUGS

Drugs today are obtained from several sources. Some sources of drugs are discussed below. Some drugs are listed under the sources. The specific drugs mentioned are not the only drugs obtained from that source.

a. **Plants**. For thousands of years, plants have served as sources of drugs. Ephedrine, a drug used to treat nasal congestion, was used by the Chinese long before western man visited the Orient. Belladonna (or Deadly Nightshade), the source of atropine and scopolamine was used in the Middle Ages. Its name means "beautiful woman" in Italian. A solution obtained by soaking the belladonna plant in water caused the pupils of the eye to dilate and appear black. These were symbols of beauty at the time. Belladonna was a favorite poison. Opium, a product obtained from the poppy plant, is mentioned in early Greek mythology as a sleep producer.

b. **Animals**. Animals provide us with large supplies of natural products like hormones. Insulin, used in the treatment of diabetes mellitus, used to be obtained from the pancreas of pork, beef, and even fish. Heparin, a potent anticoagulant, is obtained from the intestinal and lung mucosa of beef and hogs.

c. **Minerals**. Minerals, such as iron and iodine, are essential for normal growth and development. An old remedy for pallor (a very pale complexion) was the water used to cool horseshoes in the blacksmith shop. This water contained small amounts of iron in solution.

d. **Microorganisms.** You are probably aware of the fact that microbes can cause disease and/or death. Fortunately, some microorganisms can be used to produce antibiotics. These antibiotics can be used to kill or stop the growth of other microbes. Furthermore, chemically treated or killed microorganisms can be used to produce vaccines.

e. **Synthetics**. Most drugs today are synthetically made. Examples of synthetically produced drugs are aspirin and the sulfa drugs.

3-4. USES FOR DRUGS

Drugs have many uses. In today’s society, the legitimate--and not so legitimate--use of drugs is wide seen. Listed and briefly discussed below are the major uses and some representative examples of drugs:

a. **To Maintain Health**. Vitamins and minerals are used and abused in the pursuit of good health.

b. **To Reverse a Disease Process.** Antibiotics and chemotherapeutic (anticancer) agents are commonly used in medicine today. Ideally we would like these agents to cure the patient.

c. **To Relieve Symptoms.** Drugs that act to relieve symptoms do not cure the patient. Instead, they help to make the patient more comfortable in order for the patient to work or function. Since only symptoms are being relieved, the body is expected to remedy the problem.

d. **To Prevent Disease.** Vaccines and toxoids are used to prevent disease. In the 1950's, many parents kept their children at home in fear of the dreaded polio disease. Today, the only time most parents think of polio is when they take their children for their periodic (and necessary) vaccinations for this still-present threat. Further, any military veteran can quickly testify to the fact that vaccinations are an essential part of the introduction to military life.

e. **To Prevent Pregnancy**. The old saying that an ounce of prevention is better and cheaper than a pound of cure is most applicable here. The birth control "pill" or oral contraceptives and spermacidal agents in the form of creams, jellies, and suppositories are the drugs currently being used to prevent pregnancy.

Section III. CONSIDERATIONS OF DRUG THERAPY

3-5. FACTORS THAT INFLUENCE DRUG DOSAGE EFFECTS

Many factors influence how a dose of a particular drug will affect a patient. Since not all patients are the same size, weight, age, and sex, it would be wise to consider how these factors might influence how much drug a person should receive and the effect(s) that drug might have on the patient. The usual recommended adult dose of medication, as found in standard references, is based on the assumption that the patient is a "normal" adult. Such a "normal" (or average) adult is said to be 5 feet 9 inches (173 centimeters) tall and weigh 154 pounds (70 kilograms). However, many people do not fit into this category. Therefore, the following factors should be considered when patients receive drugs:

a. **Weight.** Obese (overweight) patients may require more medication than thin patients may because the drug has more tissue to which it can go. The dosage of many drugs is calculated on a weight basis. For example, a person might be prescribed a drug that has a dosage of 5 milligrams of drug per pound of patient body weight.

b. **Surface Area.** A person's height and weight are related to the total surface area of his body. The "normal" (average) adult has a body surface area of approximately 1.73 square meters. A nomogram (see Subcourse MED8O2, Pharmaceutical Calculations) is used to determine the surface area of a patient. The dosage of certain drugs (for example, the anticancer drugs) is determined by the patient's body surface area.

c. **Age**. As a rule, the very young and the elderly require less than the normal adult dose of most medications. Part of this requirement for less medication is due to the altered metabolism of the drug. Since body enzyme systems greatly influence drug metabolism, considering the differences in these enzyme systems based upon age is important. In the infant, some enzyme systems are not yet fully developed. On the other hand, the enzyme systems of the elderly may not function as well as in the past. Although several formulas are available for calculating a child's dose of medication, the two most accepted methods are those based upon the patient's weight (that is, milligrams per kilogram of body weight) or body surface area (that is, milligrams per square meter of surface area).

d. **Sex.** Physiological differences between the sexes may influence the dose or the requirement for drugs. Since females have proportionately more fat tissue than males, drugs, which have a high affinity (likeness) for fat, may require larger doses in females. Moreover, estrogen and testosterone, two sex hormones, can affect the patient's rate of metabolism which can, in turn, influence the rate at which a drug is metabolized, absorbed, or excreted from the body. The requirement for iron is much higher in the female than in the male, because of the loss of blood in each menstrual cycle.

e. **Genetic Factors**. Various racial and ethnic groups have differences in some metabolic and enzyme systems which can affect the utilization of drugs.

f. **Physical Condition of the Patient**. The physical condition of the patient influences how a particular drug might act. Consequently, the weak or debilitated patient might require smaller doses of some medications. Patients who are in extreme pain may require larger doses of analgesic agents than those patients who are in less pain.

g. **Psychological Condition of the Patient.** The patient's attitude about his disease or treatment can influence the effectiveness of a drug. It has been shown that patients receiving placebo tablets (tablets that contain no active ingredient) sometimes have the same side effects as the patients who were taking tablets of the same appearance that did contain the drug. In some cases, both types of patients (those taking the placebo and those taking the drug) recovered at the same time.

h. **Tolerance**. The therapeutic effects of some drugs are lessened in individuals after the drugs have been used for long periods. Thus, an individual who has used such a drug for a long time needs larger doses of the drug than he did when he first began to take it in order to obtain the same effect. This effect is called tolerance. Persons who use opium, heroin, cocaine, amphetamines, and barbiturates develop a tolerance to these substances. Cross-tolerance occurs when the use of one drug causes a tolerance to another drug. Alcoholics, barbiturate addicts, and narcotic addicts develop a cross-tolerance to sedatives and anesthetics.

i. **Time of Administration.** The time when a drug is administered is important. Some orally administered medications should be taken before meals (that is, on an empty stomach) to increase the amount of drug absorbed into the system. Other oral medications (that is, those that cause irritation to the gastrointestinal tract) should be taken after meals on a full stomach.

j. **Drug Interaction**. The interaction between two or more drugs may influence the overall effectiveness of each of the drugs.

(1) Synergism. Synergism is the joint action of drugs. That is, their combined effects are greater than the sum of their independent effects. Concurrent administration (giving both drugs at the same time) of synergists may require that the dose of each drug be lowered. In the case of synergism, 1 + 1 = 2 1/2. Synergism may be beneficial or harmful. Beneficial effects may be obtained when combining two potentially toxic drugs to achieve the desired therapeutic effect without causing harm to the patient. Harmful effects may occur when alcohol and some depressants are combined.

(2) Additive. In an additive drug interaction, the combined effects are equal to the sum of the independent effects of the drugs. In the case of the additive effect, 1 + 1 = 2.

(3) Antagonism. Antagonism is the canceling effect of one drug upon another. A sedative administered with a stimulant may antagonize or cancel the effects of the stimulant. Of course, the degree of antagonism varies from complete cancellation of the effect to varying degrees of reduced effectiveness.

k. **Routes of Administration**. Drugs may be given to patients using a variety of methods. Some drugs are only effective if they are given in a particular dosage form. Other drugs are administered in forms that enhance or decrease their effect or localize the drug effects.

(1) Oral. Most drugs available today can be administered by mouth (orally). Drugs can be orally administered in the form of tablets, capsules, powders, solutions, or suspensions. Drugs administered by the oral route are usually taken for their systemic effect. These medications must pass through the stomach and be absorbed in the intestinal tract. Orally administered medications are usually easy to take and are usually less expensive than other dosage forms.

(2) Sublingual/buccal. The sublingual/buccal route of administration is closely related to the oral route; however, in the sublingual/buccal route the dosage form is not swallowed. The tablet is to be dissolved under the tongue (sublingual) or in the pouch of the cheek (buccal). The drugs administered in this manner are rapidly absorbed and have the advantage of bypassing the gastrointestinal tract. Nitroglycerin, for heart patients, in tablet form is more likely the most frequently administered sublingual drug.

(3) Rectal. Drugs administered by the rectal route may have a local effect (as for hemorrhoids) or a systemic effect (as in the prevention of nausea and vomiting). The rectal route is convenient to use in pediatric patients (children) or in patients who are unconscious or vomiting. The amount of drug absorbed in the rectal route is usually less than if the drug were administered orally. The absorption of drugs administered rectally is unpredictable and can vary among patients.

(4) Vaginal/urethral. Drugs administered using the vaginal/urethral route are used for their local effect. That is, they are usually given to treat an infection or other pathological condition. Drugs administered in this route should not be irritating since systemic absorption may occur.

(5) Inhalation. Drugs administered by inhalation have either may a local or systemic effect. Anesthetics, like nitrous oxide, are inhaled and exert their effect after absorption into the circulatory system. Sprays for nasal congestion have their effect on the tissue in the nose and do not necessarily enter the general circulation.

(6) Topical. The topical route is probably the oldest route of administration. Topical medications are applied directly upon the skin. As long as the skin is intact (not broken or cut), drugs applied in this manner exert a local effect. The base (vehicle) used to carry the ingredients in the local preparation can influence the action of the drug. For example, dimethylsulfoxide (DMSO) will readily penetrate the skin and carry the active ingredient along with it.

(7) Parenteral. The term parenteral literally means to avoid the gut (gastrointestinal tract). Thus, parenterals are injectable drugs that enter the body directly and are not required to be absorbed in the gastrointestinal tract before they show their effect. Parenteral routes of administration usually have a more rapid onset of action (show their effects more quickly) than other routes of administration. Parenteral products must be sterile (free from living microbes). The parenteral route of administration does have its disadvantages: it hurts, it is not a convenient route, and once administered the injected drug cannot be retrieved.

(a) Intravenous (IV). The injection of a drug directly into the patient's veins is the most rapid route of administration. This type of parenteral route results in the most rapid onset of action.

(b) Intraarterial. In this parenteral route, the drug is injected directly into the patient's arteries. This route is not frequently used.

(c) Intrathecal. The intrathecal route involves the administration of a drug directly into the spine (subarachnoid space) as in spinal anesthesia. The intrathecal route is used because the blood-brain barrier often precludes or slows the entrance of drugs into the central nervous system.

(d) Intramuscular (IM). The intramuscular route is used when drugs are injected deeply into muscle tissue. If the drug is in aqueous (water) solution, absorption is rapid. However, if the drug is in an oily liquid or in the form of a suspension, it can prolong the release of the drug.

(e) Intradermal (ID). In this route, the drug is injected into the (top few layers) of the skin. Ideally, the drug is placed within the dermis. The intradermal route is used almost exclusively for diagnostic agents.

(f) Subcutaneous (Sub-Q/SC). This route involves the injection of the drug under the skin into the fatty layer, but not into the muscle. Absorption of the drug is rapid. Insulin is normally administered subcutaneously.

3-6. TYPES OF ADVERSE REACTIONS TO DRUGS

A patient will sometimes have an adverse reaction to a drug. Adverse reactions can have a direct toxic effect on various systems of the body or the adverse reactions can occur in the form of milder side effects.

a. **Direct Toxicity**.

(1) In general terms, toxicity refers to the poison-like effects certain substances can produce in the body. Fortunately, most drugs do not produce toxic effects in most patients. However, when some drugs are administered to a patient over prolonged periods or when some drugs are given in high dosages, direct toxic effects can result. Direct toxicity may involve one or more of the body's systems. Certain parts of the body (that is, bone marrow) produce red and white blood cells. If a toxic accumulation of a substance affects these parts of the body, blood dyscrasias (the formation of malformed or destroyed white or red blood cells) may occur.

(2) The liver has as one of its main functions the detoxification of chemical substances when they are absorbed. If these substances damage the liver significantly, its ability to detoxify them if greatly affected. Of course, if these substances are not detoxified, the concentration of the substance in the body (that is, blood stream) constantly increases. Thus, hepatotoxicity (the destruction of the cells of the liver) can result in the accumulation of toxic products to the point that other body systems are affected.

(3) The kidneys are responsible for eliminating water-soluble toxic products (that is, waste products from cellular respiration) from the bloodstream. If nephrotoxicity (damage to the kidneys) results, the accumulation of these toxic products can result in death.

(4) Toxic effects may not be limited to the person who is taking the drug. In the past, it has been demonstrated that some drugs will cross the placental barrier and enter the circulatory system of the fetus. Some drugs can exert serious effects on the developing fetus. For example, the fetus may abort or be born with any number of mental or physical defects. Since few mothers are willing to subject themselves and their unborn children to drug testing, the effects of most drugs on the fetus are unknown. Most of what is known about teratogenicity, fetal malformations, has been learned either from experimental studies with animals or from the unfortunate experiences of some mothers. The fetus is particularly susceptible to the adverse effects of medications during the first three months after conception (the first trimester). Unfortunately, many women do not realize they are pregnant until they are well into their first trimester.

b. **Allergic Reactions**. A few individuals may be allergic, or hypersensitive, to a drug. This allergy may arise because of a prior contact with a particular substance called an allergen (it may even be the drug itself). This acquiring of an allergy is called sensitization. You should understand that the symptoms of an allergy are not related to the ordinary effects of the drug. Allergic reactions to a drug may range from a mildly irritated skin rash to anaphylaxis (a fatal shock). It has been shown that penicillin, a widely prescribed antibiotic, produces varying types of allergic reactions in from 1 to 10 percent of the patients who are administered the drug.

c. **Side Effects**. Most drugs do not produce only one single effect. Instead, they may produce several physiological responses at the same time. For example, antihistamines, drugs frequently used for their anti-allergic action tend to produce drowsiness. In this case, drowsiness is a side effect of the antihistamines. With some drugs, the side effects are so worrisome and inconvenient that the patient may stop taking the medication.

d. **Drug Dependence.** All drugs have the potential of producing dependence, the need to have that drug. There are two major types of dependence: psychological and physiological.

(1) Psychological dependence may occur after a patient has been taking a medication for a long time. With psychological dependence, the patient becomes so convinced that he needs the drug (in order to continue to lead an improved life) that he will go to great lengths to ensure that he receives the medication. Patients habituated to amphetamines may demonstrate this type of dependence. Psychological dependence is very difficult to treat.

(2) With physiological dependence, the patient's body develops a real need for the drug over a long period. Since there is a physiological need for the drug, the body reacts by going through withdrawal symptoms (that is, tremors, nausea, vomiting, and convulsions) if the drug is suddenly withheld. The patient habituated to narcotics and barbiturates have physiological dependence.

Section IV. FACTORS WHICH INFLUENCE DRUG ACTION

3-7. INTRODUCTION TO PHARMACOKINETICS

Pharmacokinetics deals with the absorption, distribution, metabolism (biotransformation), and excretion of drugs. Any time a drug is administered, these factors will directly affect the amount of drug that will arrive at the site where the drug acts. The amount of drug at the site of action will determine both the intensity of drug action and the length of time the drug will show its effect(s).

3-8. ABSORPTION OF DRUGS

Absorption involves the uptake of the drug by the body. Three factors affect the absorption of a drug: its water solubility, its fat solubility, and the transport mechanisms of the body. It is imperative that you understand that all drugs must be in solution before they can be absorbed.

3-9. FACTORS WHICH AFFECT ABSORPTION

a. **Water Solubility**. All body fluids are water based. Therefore, a drug must be soluble in water in order to be absorbed. Dissolution of the drug in aqueous (water) solution is dependent 6n the pH of the solution and the disintegration of the drug.

(1) Disintegration. Disintegration (figure 3-1) increases the surface area of a drug. The speed at which a dosage form disintegrates is dependent upon the type of solid dosage form and the manufacturing process used to make that dosage form. The solid dosage form could be a tablet, suppository, capsule, powder, or suspension. Take a tablet for example. The manufacturer may add starch to the tablet in order to make it swell when it is added to water. The tablet may be a sublingual tablet that is made to rapidly dissolve in the mouth. On the other hand, the manufacturer may compress the contents of the tablet under great pressure so that it will slowly dissolve. Further, an enteric coating may be applied to the tablet so that it will dissolve in the intestine. In the case of some capsules, "tiny time capsules" systematically dissolve during a period and prolong the effect of the drug.

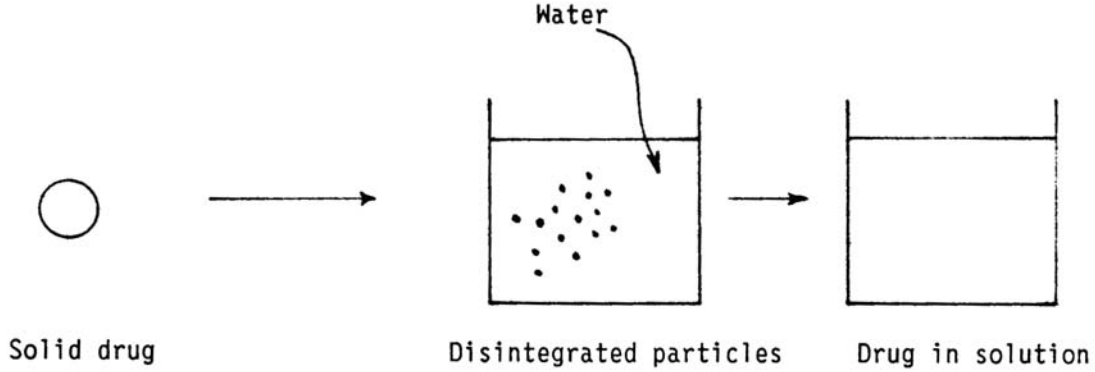


Figure 3-1. Dissolution of a drug.

(2) pH. The relative acidity or basicity of the fluids into which a drug is placed will affect how rapidly the drug will dissolve. The pH of the stomach can be as low as 1.0 (very acidic), the pH of the small intestine can range from 6.9 to 7.4 (slightly acidic to slightly basic), while the pH of the plasma is approximately 7 4 (slightly basic). Weakly acidic drugs (that is, aspirin) are more soluble in a basic or alkaline solution like the small intestine (pH above 7.4). Weakly basic drugs, such as tetracycline hydrochloride, are more soluble in an acidic solution like the stomach (pH below 7.0).

(3) Ionization. Ionization is the process whereby a substance breaks down into positively and negatively charged particles (figure 3-2).

(a) For example, when hydrochloric acid ionizes, it forms hydrogen ions (H+) and chloride ions (Cl-).

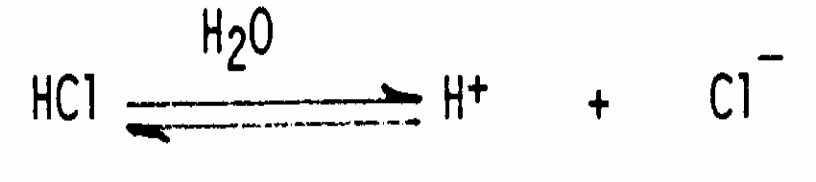


Figure 3-2. The ionization of hydrochloric acid.

(b) Equilibrium is established based on the chemical nature of each drug. That is, a certain percentage of the drug ionizes, while the rest remains as the compound. In summary, dosage forms must go into solution. A solid dosage form must disintegrate and dissolve before it can be absorbed. A suspension dosage form has already been partially dissolved; the drug particles must dissolve before absorption can occur. A solution dosage form contains a drug that has already been dissolved; thus, no disintegration or dissolution is required before absorption can occur.

b. **Fat Solubility**. In the last area, the topic of water solubility was discussed. For instance, a drug is in solution. What other factors must it overcome in order to be absorbed? One is fat solubility. Almost without exception, all body membranes are lipid (fatty) in nature. Membranes separate even the various water compartments of the body. These membranes are selectively permeable. That is, these membranes will only allow certain materials to pass through them. In particular, the membranes favor the absorption of unionized particles (particles which have neither a positive nor a negative charge).

c. **Transport Mechanisms**. The body either in an active or in a passive way can absorb drugs.

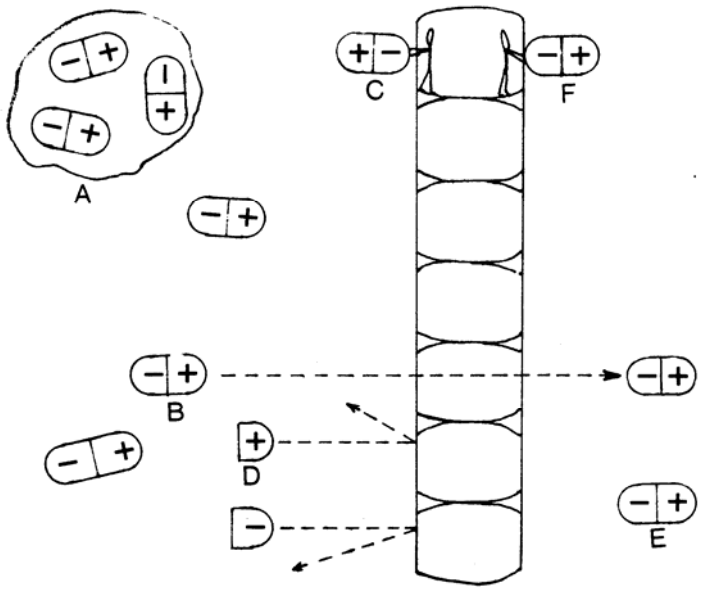
(1) Passive transport. Passive transport (diffusion) follows a concentration gradient. That is, if there is a high concentration of a substance on one side of the barrier and a low concentration of that substance on the other side of the barrier, nature tries to balance the two concentrations so that one is equal to the other. The two concentrations can be equalized in one of two ways. One way is for the liquid containing the substance to move from the side with fewer particles to the side with more particles. This process, called osmosis, will ultimately result in the two sides having the same concentration. The second option is for the drug particles to move from the side of higher concentration to the side of the lower concentration. This process, called diffusion, will also ultimately result in the two sides having the same concentration. Most drugs are absorbed in this manner of diffusion. With diffusion, the drug particles move from the side of higher concentration through the cell membrane into the side of lower concentration.

(2) Active transport.

(a) A ride in a roller coaster would give you a background to understand this section on active transport. You have probably observed that a roller coaster car does not have an engine. Common sense would tell you that the car does not need an engine to go down the hills, but up those hills--that is a different story. You have probably observed that a mechanism exists for pulling the car up the hill.

(b) Active transport works in much the same way. Proteins (in the cells) make up the linings of the cells. Some of these proteins have a particular affinity (attraction) for a selected drug. When the drug molecule meets the cell wall, the protein called a "carrier molecule" attaches itself to the drug, carries it across the cell membrane, and releases the drug on the other side. The drug then enters the circulation and is distributed throughout the body. Active transport can move against a concentration gradient to move a substance to a place of higher concentration. Vitamin B-12 is an example. Very little of this vitamin can pass through the intestinal wall of the gut by diffusion; however, a carrier molecule, often called "intrinsic factor" transports the vitamin across the gut. Once in circulation, the vitamin is stored in the liver. The concentration of drug in the liver is several hundred times higher than in circulation. Therefore1 if a drug is unionized, water soluble, and fat-soluble, it may pass through the cells of the gut if taken orally. Once in circulation, the drug must pass through the fatty layer of the individual cell in order to have an effect. So, even injected medications have some of the same problems as oral medications.

(3) Illustration of concepts. Perhaps some insight can be gained about this whole topic of drug transport mechanisms if a diagram depicting the concepts is shown and discussed. Figure 3-3 is provided for this purpose. In the figure, several concepts are illustrated:



NOTE: Passive transport or diffusion has absorbed Molecule B. Once it has been absorbed, the circulating blood will carry it away. Consequently, the concentration of the drug will always remain higher in the gut and diffusion will continue. As the unionized particles are absorbed, the ionized particles will attach to each other to form more unionized drug. This occurs because the drug has equilibrium established between the ionized and unionized form; as the unionized form is removed, the balance shifts make up for the loss. Molecules C and F are being moved by active transport. They must also be unionized and fat soluble; however, their transport does not rely on differences in concentration. This transport process also accounts for the absorption of a drug by the individual cells within the body.

Figure 3-3. Illustration of drug transport concepts.

(a) A--Drug A is an undissolved drug. It is not in solution and it cannot be absorbed.

(b) B--B is a molecule of a drug in solution. It is unionized and can be absorbed.

(c) C--C is a molecule of a drug attached to a "carrier molecule" at the cell wall.

(d) D--D is an ion of a drug. It cannot be absorbed since the fatty layer repels it.

(e) E--E is a molecule of a drug. It is in circulation and will be carried away.

(f) F--F is a molecule of the drug that is being released into circulation by a carrier molecule.

3-10. DISTRIBUTION OF DRUGS

a. Once the drug is absorbed, it enters the circulation and is carried throughout the body. The location in the body where the drug goes varies from drug to drug. The drug may be stored in bone or fat, bound to the proteins in the blood plasma, or circulate freely as the unbound drug. The drug will find its way into many organs. Finally, some of the drug will reach the target tissue where it can cause the effect for which it was administered. An equilibrium will be established between the circulating unbound drug and each area of the body.

b. The distribution of a drug in the body happens in a very systematic manner. figure 3-4 demonstrates the concept of distribution.

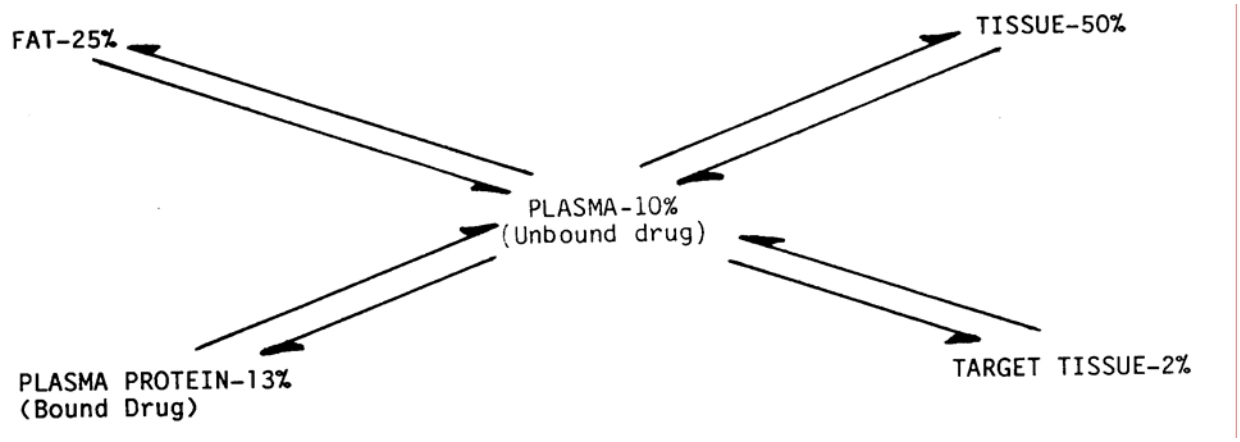


Figure 3-4. Drug distribution within the body.

c. Assume that 100 micrograms (100 mcg) of a drug have been absorbed and is distributed based on the percentages noted in figure 3-4. Of the 100 micrograms absorbed, only two micrograms of the drug will arrive at the target tissue to give the desired pharmacological effect. If two micrograms is enough drugs to produce the desired pharmacological effect, the desired effect will be obtained. However, if the amount of drug required to produce the effect is four micrograms, the desired pharmacological effect will not be obtained. The dose of the drug can be increased so that 200 milligrams of the drug can be absorbed, thus providing the amount of drug needed to give the desired pharmacological effect. However, doubling the dose may present problems. Doubling the dose would also double the amount of drug in the other areas of the body. Perhaps this increased dosage may produce some response by another body organ. For example, the patient may become nauseous, vomit, lose his hair, or go into convulsions. These are side effects of the drug. Thus, it is important to remember that the whole body must be taken into account when a drug is administered. If the problem of the side effects cannot be resolved, the drug may not be released for use.

NOTE: Another areas of concern in the distribution of drugs are those that crosses the placental barrier. Drugs may actively or passively cross the placental barrier and enter the fetal circulation. The enzyme systems of the developing fetus may not be able to adequately metabolize the drug. Toxic effects can result. At this time, it is virtually impossible to predict whether a drug will pass the placental barrier.

3-11. METABOLISM (BIOTRANSFORMATION)

The process of drug absorption and distribution is dynamic. That is, it is continually changing. Even as the drug is being distributed, the individual cells of the body begin to chemically change or alter the drug. This metabolic process of changing the drug is called metabolism or biotransformation. While many cells of the body will be involved in this process, the liver is the organ primarily responsible for this biotransformation. The liver changes drugs to make them more water-soluble so that they may be more easily excreted from the body. During the process of metabolism, a drug may be rendered inactive, converted from an inactive form to an active one, or be made more toxic. The liver may oxidize, reduce, hydrolyze, or conjugate (bind with a protein) the drug. The kidney will also play an active role in conjugating drugs.

3-12. BIOAVAILABILITY

a. The term bioavailability was defined in the first portion of this subcourse. In figure 3-4, all 100 micrograms of the drug was available to the system, since it was absorbed. The amount of drug originally administered to the patient was not stated. That amount of administered drug could have ranged from 100 micrograms to 1000 milligrams or more. From the reading, you should have noted that absorption is not an easy process, and that any number of things can interfere with the process.

b. The controversy concerning generic drugs deserves consideration at this point. For example, switching a patient from one generic brand of ampicillin to another brand of ampicillin could cause some problems for some patients. Thus, one company's generic brand of a drug might not be able to be absorbed as quickly as another company's generic brand of the same drug. With other drugs and some patients the switch from one company's drug to another company's drug is of little consequence.

c. Drugs that present the most problems in terms of bioavailability are oral solids. That is because oral solids must disintegrate, dissolve, be water soluble, be fat soluble, unionize, and pass through the drastic pH changes from the stomach to the small intestine.

3-13. EXCRETION

a. The term bioavailability was defined in the first portion of this subcourse. In figure 3-4, all 100 micrograms of the drug was available to the system, since it was absorbed. The amount of drug originally administered to the patient was not stated. That amount of administered drug could have ranged from 100 micrograms to 1000 milligrams or more. From the reading, you should have noted that absorption is not an easy process and that any number of things can interfere with the process.

b. The inability of a patient to excrete drugs and other waste can be life threatening. The elimination of drugs through sweat, saliva, and the lungs is of minor interest in this subcourse. Of course, the excretion of drugs in breast milk is of concern to mothers who breast-feed their infants. As a rule, drugs that are weakly basic are more likely to be excreted in breast milk, because the milk is slightly acidic; therefore, the basic drugs are more soluble in breast milk.

c. Patients who have limited liver and kidney function usually require lower doses of medication. This is because more of the drug tends to stay in the body.

3-14. MECHANISMS OF DRUG ACTION

a. **Receptor Site Theory**. A drug that finally enters a cell may produce an effect. It is able to produce this effect by a variety of complex biochemical processes. Most of the processes can be simplified into one explanation of the mechanism of drug action known as the receptor-site or "lock and key" theory. This theory states that a drug (the key) combines with a receptor-site (the lock) to produce a pharmacological effect. Drugs that will fit into the receptor-site are said to have an "affinity" for that receptor-site. Only drugs that fit into the receptor-site will produce a pharmacological response. Figure 3-5 visually represents the receptor-site theory.

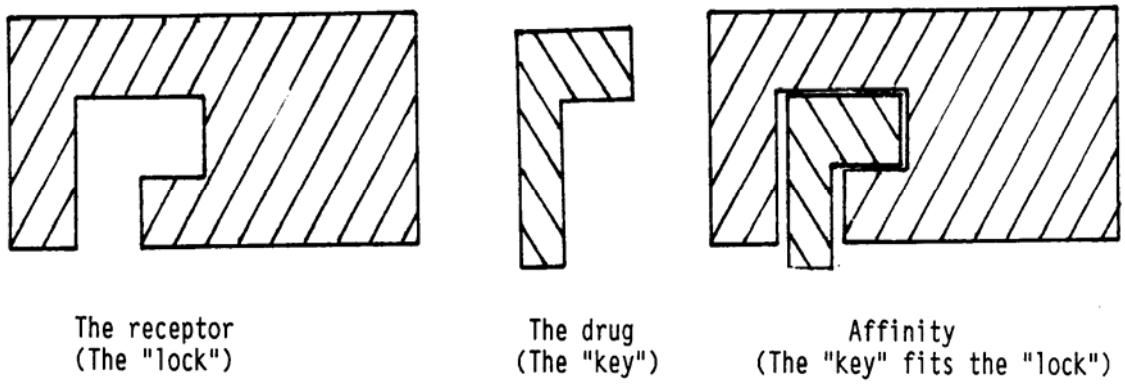


Figure 3-5. The receptor-site theory.

b. **Chemical Structure Activity Relationship**. As a review, drug molecules have specific chemical structures. The chemical structure of a drug will determine if a drug molecule (the key) will fit into the receptor-site (the lock) and produce a pharmacological effect. For example, whether the hydroxyl (OH-) group is on the left or right side of the molecule or is at a 520 angle with the molecule can determine whether the "key" will fit the "lock." This is referred to as chemical structure activity relationship. From this, we can say that drugs that are similar in composition and chemical structure may have similar effects. The chemical structure of a drug can be altered with no effect upon the pharmacological effect the drug produces. However, the change in the chemical structure of the drug molecule can increase or decrease its side effects. Further, the modification of a drug molecule can influence its pharmacological actions. Therefore, the modification of a drug's molecular structure can result in the formation of a drug that can produce a desired pharmacological effect with a significantly lower dose and with an accompanying decrease in undesired side effects.

c. **Antagonists**. Antagonists are drugs that will or reverse block the action of other drugs. There are two types of antagonists: competitive and physiological.

(1) Competitive antagonists. Competitive antagonists combine with the receptor-site and prevent another drug from combining with the receptor-site. A competitive antagonist does not displace a drug at the receptor-site. Figure 3-6 illustrates the concept of a competitive antagonist.

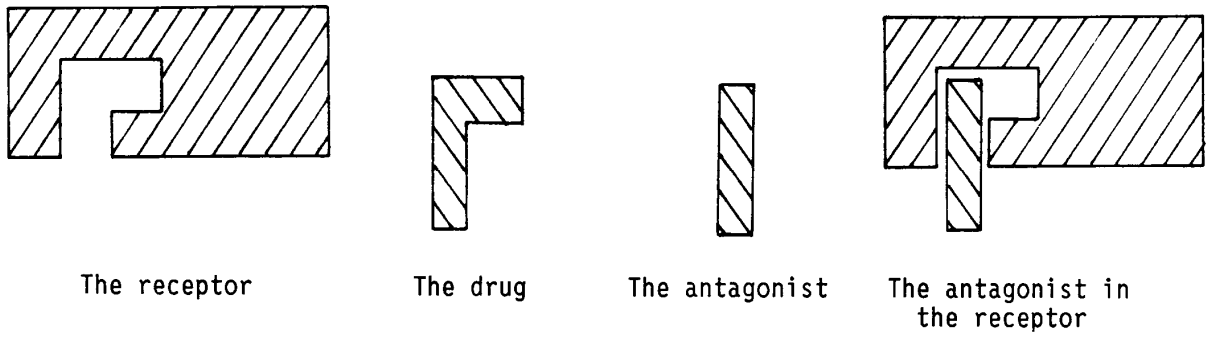


Figure 3-6. A competitive antagonist.

(2) Physiological antagonists. Physiological antagonists reverse the action of the drug by acting on a different receptor-site to cause a different physiological effect.

3-15. DRUG EFFICACY

a. Drug efficacy refers to the effectiveness of a drug. Drug efficacy is measured by the clinical response of the patient. A drug is considered to have a high degree of efficacy, if it achieves desired clinical results.

b. Laboratory tests may be used to determine the amount of drug that has been absorbed. The amount of drug absorbed may be used to predict a patient's response. However, since people respond differently to the same dose of the same drug, merely knowing the amount of drug absorbed does not always indicate the response of an individual patient.

c. A general rule is that as the dose of a drug is increased, a greater effect is seen in the patient until a maximum desired effect is reached. If more drug is administered after the maximum point is reached, the side effects will normally increase. figure 3-7 illustrates this principle.

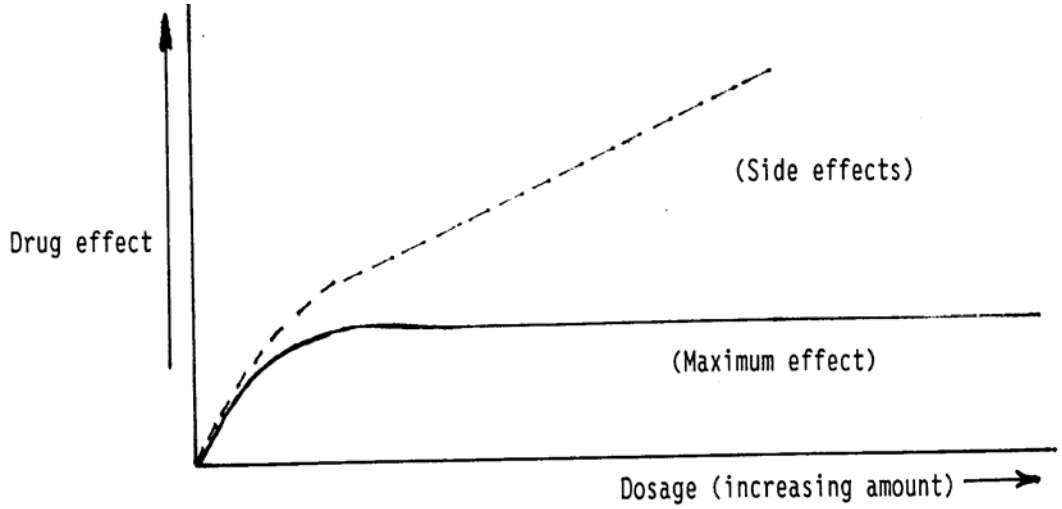


Figure 3-7. Relationship between dosage and drug effect.

Continue with Exercises

EXERCISES, LESSON 3

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the definitions below, select the definition of the term drug.

   a. A substance that is used to cure all diseases.

   b. A substance used to prevent, diagnose, or treat disease or to prevent pregnancy.

   c. A substance that can only be purchased at a drugstore.

   d. A substance that occurs naturally and cannot cause any toxic reactions.

2. From the definitions below, select the definition of the term toxicology.

   a. The science of chemicals.

   b. The science of drugs.

   c. The science of poisons.

   d. The science of dosage.

3. Select the drug that is derived from an animal source.

   a. Belladonna.

   b. Heparin.

   c. Iron.

   d. Aspirin.

4. Select the statement that best describes a use of drugs.

    a. To produce anxiety or tension.

    b. To relieve the symptoms of a disease or condition.

    c. To cure diabetes.

    d. Both a and b.

    e. Both b and c.

5. Select the statement that best describes how the physical condition of a patient might influence the amount of drug required to obtain a specific effect.

    a. Debilitated patients always require the same amount of drug as a healthy person.

    b. The physical condition of a patient never influences the required dose of a drug.

    c. The weak patient might require smaller doses of a drug to achieve an effect.

    d. Patients in extreme pain usually require smaller doses of analgesic agents rather than patients who are in less pain.

6. Select the statement that best describes drug dependence.

    a. Drug dependence occurs whenever a patient takes a particular drug for a long period.

    b. Drug dependence is said to occur when the patient has either a physiological or psychological need for a drug.

    c. Drug dependence occurs when a patient's body requires a drug, but cannot tolerate its harmful effects.

    d. Drug dependence can only occur with certain types of drugs (like narcotics).

7. Select, from the list below, the definition of the term synergism.

    a. Synergism occurs when one drug lives off another drug.

    b. Synergism occurs when the combined effect of two drugs is greater than the sum of their independent effects.

    c. Synergism occurs when the combined effects of two drugs are equal to the sum of the independent effects of the drugs.

    d. Synergism occurs when one drug's effects cancel the effects of another drug.

8. Select the route of administration in which the dosage form is placed in the mouth but not swallowed.

    a. Parenteral.

    b. Rectal.

    c. Sublingual/Buccal.

    d. Oral.

9. Select the statement that best describes the sublingual/buccal route of administration.

    a. In this route of administration, the drug is swallowed and very quickly absorbed by the patient.

    b. In this route of administration, the drugs are absorbed only after being taken into the gastrointestinal tract.

    c. In this route of administration, the drug is absorbed without passing through the gastrointestinal tract.

    d. In this route of administration, the drug is applied directly to the skin.

10. From the statements below, select the statement that best describes how fat solubility influences drug absorption.

    a. Since all body fluids are fat based, a drug must be soluble in fat in order to be absorbed and demonstrate its effect.

    b. Since body membranes are lipids in nature, a drug that will pass through lipid material will be absorbed much more quickly than ionized drug particles.

    c. The body cannot absorb a fat-soluble drug, because it is unionized.

    d. All fat-soluble drugs must be converted into water-soluble substances before they can be absorbed.

11. From the list below, select the definition of the term metabolism.

    a. The chemical process of producing a drug.

    b. The metabolic process of changing a drug.

    c. The process of transforming a living life form.

    d. The modification of complex substances to make them powerless.

12. From the list below, select the definition of the term excretion.

    a. The process of placing a drug or its metabolites into the body.

    b. The process of metabolically changing a drug or its metabolites.

    c. The process of eliminating a drug or its metabolites from the body.

    d. The process of concentrating a drug and removing it from the patient's gastrointestinal tract.

13. From the descriptions below, select the description that best describes the Receptor-Site Theory of the mechanism of drug action.

    a. A drug (the lock) combines with a receptor-site (the key) to produce a pharmacological effect.

    b. A drug (the key) combines with a receptor-site (the lock) to produce a pharmacological effect.

    c. A drug (the receptor-site) combines with cell components (the lock) to produce a pharmacological effect.

    d. A drug (the lock) combines with a receptor-site in the intestine to produce an essential effect.

14. Select the statement that best contrasts passive transport with active transport.

    a. Active transport occurs when molecules of the drug move from an area of high concentration to an area of low concentration, while passive transport occurs when a "carrier molecule" carries a drug molecule across a cell membrane.

    b. Passive transport occurs in comatose patients whose cells are unable to actively absorb drugs through the normal processes.

    c. Passive transport occurs when molecules of a drug move from an area of high concentration to an area of low concentration, while active transport occurs when a "carrier molecule" carries a drug molecule across a cell membrane.

    d. Passive transport occurs when a "carrier molecule" carries drug molecules from an area of low concentration to an area of high concentration, while passive transport involves the movement of blood plasma from a low concentration to a high concentration.

15. From a group below, select the description that best describes the importance of structure activity relationships.

    a. Drugs that are similar in composition and structure may have similar effects.

    b. Drugs that are not similar are ineffective.

    c. Drugs that are active generally have similar structures.

    d. Drugs that are similar in effect generally have the same trade name.

16. Select the statement that best contrasts competitive antagonist with physiological antagonists.

    a. Competitive antagonists combine with the receptor-site and prevent another drug from combining with the receptor-site, while physiological antagonists reverse the action of a drug by acting on a different receptor-site to cause different physiological reaction.

    b. Competitive antagonists produce pharmacological effects by producing a physiological effect different from the drug, while physiological antagonists physiologically compete for a spot on the receptor-site.

    c. Competitive antagonists combine with the receptor-site and remove the drug from the site, while physiological antagonists physically compete for the receptor-site.

    d. Physiological antagonists physically remove drug molecules from the receptor-site, while competitive antagonists compete for the receptor-site.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 3

1. b (para 3-2a)
2. c (para 3-2e)
3. b (para 3-3b)
4. b (para 3-4c)
5. c (para 3-5f)
6. b (para 3-6)
7. b (para 3-5j(1))
8. c (para 3-5k(2))
9. c (para 3-5k(2))
10. b (para 3-9b)
11. b (para 3-11)
12. c (para 3-13a)
13. b (para 3-14a)
14. c (para 3-9c(1) and (2))
15. a (para 3-14b)
16. a (para 3-14c(1) and (2))

End of Lesson 3

LESSON ASSIGNMENT

LESSON 4 Local Anesthetic Agents.

TEXT ASSIGNMENT Paragraphs 4-1--4-8.

LESSON OBJECTIVES After completing this lesson, you should be able to:

4-1. Given one of the following terms: local anesthetic, local infiltration, topical block, surface anesthesia, nerve block, peridural, and spinal anesthesia, and a group of statements, select the meaning of that term.

4-2. From a group of statements, select the statement that best describes the mechanism of action for local anesthetics.

4-3. Given a group of statements, select the statement that best describes why vasoconstrictors are used in conjunction with local anesthetics.

4-4. From a group of statements, select the caution and warning associated with the use of a local anesthetic combined with a vasoconstrictor.

4-5. Given a group of statements, select the statement that best describes why hyaluronidase (Wydase^{R}) is used in conjunction with local anesthetics.

4-6. Given a group of statements, select the statement that describes a caution and warning associated with the use of local anesthetics.

4-7. From a list of toxicities, select the toxicity associated with the use of local anesthetics.

4-8. Given the trade name of a local anesthetic agent and a list of generic names, match the trade name of the agent with its generic name.

4-9. Given the trade and/or generic name of a local anesthetic agent and a group of possible uses or cautions and warnings, select the clinical use or caution and warning associated with that agent.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 4

LOCAL ANESTHETIC AGENTS

Section I. BACKGROUND INFORMATION

4-1. BACKGROUND INFORMATION

In order to understand what a local anesthetic is and how it is used, you need to study/review the following definitions:

a. **Local Anesthetic**. A local anesthetic is an agent that interrupts pain impulses in a specific region of the body without a loss of patient consciousness. Normally, the process is completely reversible--the agent does not produce any residual effect on the nerve fiber.

b. **Local Infiltration (Local Anesthesia)**. Local infiltration occurs when the nerve endings in the skin and subcutaneous tissues are blocked by direct contact with a local anesthetic, which is injected into the tissue. Local infiltration is used primarily for surgical procedures involving a small area of tissue (for example, suturing a cut).

c. **Topical Block**. A topical block is accomplished by applying the anesthetic agent to mucous membrane surfaces and in that way blocking the nerve terminals in the mucosa. This technique is often used during examination procedures involving the respiratory tract. The anesthetic agent is rapidly absorbed into the bloodstream. For topical application (that is, to the skin), the local anesthetic is always used without epinephrine. The topical block easily anesthetizes the surface of the cornea (of the eye) and the oral mucosa.

d. **Surface Anesthesia**. This type of anesthesia is accomplished by the application of a local anesthetic to skin or mucous membranes. Surface anesthesia is used to relieve itching, burning, and surface pain (for example, as seen in minor sunburns).

e. **Nerve Block**. In this type of anesthesia, a local anesthetic is injected around a nerve that leads to the operative site. Usually more concentrated forms of local anesthetic solutions are used for this type of anesthesia.

f. **Peridural Anesthesia.** This type of anesthesia is accomplished by injecting a local anesthetic into the peridural space. The peridural space is one of the coverings of the spinal cord.

g. **Spinal Anesthesia.** In spinal anesthesia, the local anesthetic is injected into the subarachnoid space of the spinal cord.

4-2. MECHANISM OF ACTION OF THE LOCAL ANESTHETICS

a. The nerve fiber is a long cylinder surrounded by a semipermeable (allows only some substances to pass) membrane. This membrane is made up of proteins and lipids (fats). Some of the proteins apparently act as channels, or pores, for the passage of sodium and potassium ions through the membrane.

b. The movement of nerve impulses along a nerve fiber is associated with a change in the permeability of the membrane. The pores widen, and sodium ions (Na+) move to the inside of the fiber. At the same time, potassium ions (K+) diffuse out through other pores (see figure 4-1). The entire process is called depolarization. Immediately after the nerve impulse has passed, the pores again become smaller. Sodium ions (Na+) are now "pumped" out of the fiber. At the same time, potassium ions are actively transported into the fiber. The nerve membrane is then ready to conduct another impulse.

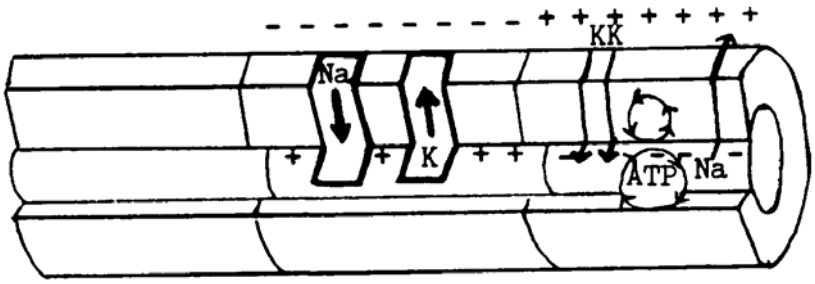


Figure 4-1. Mechanism of nerve impulse transmission.

c. Local anesthetics block depolarization of the nerve membrane. That is, to make the conduction of the nerve impulse impossible.

d. The local anesthetic effect lasts as long as the agent maintains a certain critical concentration in the nerve membrane. There is a potential problem: the local concentration needed to prevent conduction of the nerve impulse is much greater than the tolerable blood level. *TO AVOID A SYSTEMIC TOXIC REACTION TO THE LOCAL ANESTHETIC, THE SMALLEST AMOUNT OF THE MOST DILUTE SOLUTION THAT WILL EFFECTIVELY BLOCK THE PAIN SHOULD BE ADMINISTERED.*

4-3. THE USE OF VASOCONSTRICTORS IN CONJUNCTION NITH LOCAL ANESTHETICS

a. **Indications.** Vasoconstrictors (like epinephrine) are sometimes used in conjunction with local anesthetics. Vasoconstrictors are used to prolong the duration of action of local anesthetics. Vasoconstrictors also help to control bleeding. Furthermore, the vasoconstrictor delays the absorption of the local anesthetic by reducing the blood flow to the affected area. This results in a reduction of the toxic effects of the local anesthetic, since the rate of absorption keeps pace with the rate the local anesthetic is metabolized by the body. Vasoconstrictors are of no value in delaying the absorption of the local anesthetic from mucous membranes (that is, topical blocks).

b. **Cautions and Warnings of the Combination**.

(1) It should be recognized that the injection of epinephrine-containing solutions in or around fingers, toes, and the penis is not recommended.

(2) Freshly prepared combinations of vasoconstrictors and local anesthetics are more effective than commercially premixed epinephrine-containing local anesthetic solutions. This is because a very low pH is required to stabilize the epinephrine in these mixtures. In general, the content of one part epinephrine to 200,000 parts of the local anesthetic agent (is optimum) will minimize the side effects inherent with epinephrine. Great care must be taken in calculating this dilution. Small, precisely calibrated syringes should be used in the mixing process. It should be noted that the standard solution of epinephrine supplied is a 1:1000 (1 to 1000) concentration in each glass ampule. This means that 1 milliliter of the 1:1000 epinephrine solution contains 1 milligram of epinephrine. In preparing a 1:200,000 dilution, epinephrine should be added to a local anesthetic solution on a ratio of 0.1 milliliter-20 milliliters of local anesthetic solution. This does not apply to subarachnoid injections, in which a higher concentration of epinephrine is required.

4-4. ANOTHER AGENT WHICH CAN AFFECT THE ACTIONS OF LOCAL ANESTHETICS

Hyaluronidase (Wydase®) is sometimes used in conjunction with local anesthetics. Hyaluronidase is an enzyme that breaks down the material that binds cells together. Thus, when hyaluronidase is combined with local anesthetic, greater infiltration (movement) of the local anesthetic in the tissues is made possible.

4-5. CAUTIONS AND WARNINGS ASSOCIATED WITH LOCAL ANESTHETICS

a. Precautions should be taken against the danger of confusing the various agents with one another or mistaking different concentrations of the same drug.

b. In order to avoid intravascular (into the veins) injection, aspiration in several planes with the plunger of the syringe should always be done before injecting the anesthetic solution into the tissues.

c. The instillation of local anesthetic agents into the trachea and bronchi leads to immediate absorption, which soon reach blood levels comparable to those reached by straight intravenous injection.

d. A previously punctured vial of local anesthetic solution should never be re-autoclaved.

e. Discolored local anesthetic solutions should be immediately thrown away.

4-6. TOXICITIES OF LOCAL ANESTHETICS

Essentially all systemic toxic reactions associated with local anesthetics are the result of over-dosage leading to high blood levels of the agent given. Therefore, to avoid a systemic toxic reaction to a local anesthetic, the smallest amount of the most dilute solution that effectively blocks pain should be administered.

a. **Hypersensitivity**. Some patients are hypersensitive (allergic) to some local anesthetics. Although such allergies are very rare, a careful patient history should be taken in an attempt to identify the presence of an allergy. There are two basic types of local anesthetics (the amide type and the ester type). A patient who is allergic to one type may or may not be allergic to the other type.

b. **Central Nervous System Toxicities.** Local anesthetics, if absorbed systematically in excessive amounts, can cause central nervous system (CNS) excitement or, if absorbed in even higher amounts, can cause CNS depression.

(1) Excitement. Tremors, shivering, and convulsions characterize the CNS excitement.

(2) Depression. The CNS depression is characterized by respiratory depression and, if enough drug is absorbed, respiratory arrest.

c. **Cardiovascular Toxicities**. Local anesthetics if absorbed systematically in excessive amounts can cause depression of the cardiovascular system. Hypotension and a certain type of abnormal heartbeat (atrioventricular block) characterize such depression. These may ultimately result in both cardiac and respiratory arrest.

Section II. LOCAL ANESTHETICS AND THEIR CLINICAL USES

4-7. EXAMPLES OF LOCAL ANESTHETICS

The local anesthetics you may encounter in a hospital or fields setting are described below. The discussion does not cover every fact known about the use of a particular drug. Therefore, you are encouraged to read references or to ask knowledgeable personnel your specific questions concerning points not presented in this subcourse.

NOTE: Refer to table 4-1 for an overview of the clinical uses of various local anesthetics.

	Ophthalmic Topical	Topical	Infiltration	Nerve Block	Spinal	Epidural and Caudal
1. Cocaine	X	X				
2. Procaine			X	X	X	
3. Chloroprocaine			X	X		X
4. Tetracaine	X	X			X	
5. Proparacaine	X					
6. Benzocaine		X				
7. Lidocaine		X	X	X	X	X
8. Mepivacaine			X	X		X
9. Prilocaine			X	X		X
10. Bupivacaine			X	X		X
11. Bupivacaine	X	X			X	
12. Dichlorotetra-fluorethane *		X				
13. Ethyl chloride *		X				

*Surface anesthetics for application to the skin.

Table 4-1. An overview of the clinical uses of various local anesthetics.

a. **Lidocaine Hydrochloride (Xylocaine®).**

(1) Clinical uses. Lidocaine is used as a local anesthetic for infiltrations, nerve blocks, spinal anesthesia, topical anesthesia, and for caudal and epidural anesthesia. It has a rapid onset of action and its effects last from 75 to 150 minutes. It has also been used as a cardiac depressant (anti arrhythmic).

(2) Forms available. Lidocaine is available in injection form (various percentage concentrations), jelly form, and in cream form.

b. **Mepivacaine (Carbocaine®).**

(1) Clinical uses. Mepivacaine is pharmacologically and chemically related to lidocaine. It is used for infiltration, nerve block, peridural, and regional anesthesia. The duration of action for this drug is from 2 to 2 1/2 hours.

(2) Forms available. Mepivacaine is available in injection form.

c. **Prilocaine (Citanes®).**

(1) Clinical uses. Prilocaine is pharmacologically similar to both lidocaine and mepivacaine. It is used for infiltration, nerve block, peridural, and regional anesthesia. This drug is less toxic than lidocaine because it is metabolized and excreted faster than lidocaine.

(2) Forms available. Prilocaine is available in injection form.

d. **Bipivacaine (Marcaine®).**

(1) Clinical uses. Bipivacaine is pharmacologically related to lidocaine. It is used for infiltration, nerve block, and epidural anesthesia.

(2) Forms available. Procaine is available in injection form.

e. **Dibucaine (Nupercainal®, Nupercaine®).**

(1) Clinical uses. Dibucaine is used for spinal and topical anesthesia. It is the most potent local anesthetic. It is one of the most toxic and longest-acting local anesthetics.

(2) Forms available. Dibucaine is available in cream, spray, suppository, ointment, and injection forms.

f. **Procaine (Novocaine®).**

(1) Clinical uses. Procaine is used for infiltration, nerve block, and spinal anesthesia. Procaine is not applied topically. Its duration of action is approximately 1 hour. It is a fairly safe local anesthetic to use since it is metabolized quickly.

(2) Forms available. Procaine is available in injection form.

g. **Chloroprocaine (Nesacaine®, Nesacaine-C®).**

(1) Clinical uses. Chloroprocaine is pharmacologically similar to procaine. Chloroprocaine is used for infiltration, nerve block, caudal, and epidural anesthesia.

(2) Forms available. Chloroprocaine is available in injection form.

h. **Tetracaine (Pontocaine®).**

(1) Clinical uses. Tetracaine is used for topical, nerve block, infiltration, spinal, and caudal anesthesia. Its onset of action is 15 minutes.

(2) Forms available. Pontocaine is available in injection, cream, ointment, and injectable forms.

i. **Proparacaine (Alcaine®, Ophthetic®).**

(1) Clinical uses. Proparacaine is used primarily to produce anesthesia when applied to the eye. It has a rapid onset of action (20 seconds) and its duration of action is approximately 15 minutes.

(2) Forms available. Proparacaine is supplied in solution form.

j. **Benzocaine (Americaine®).**

(1) Clinical uses. Bezocaine is used for topical anesthesia of the mucous membranes and skin. It is used in many over-the-counter spray preparations for the treatment of sunburn and itching.

(2) Forms available. Benzocaine is available in solution, ointment, and spray forms.

k. **Cocaine**.

(1) Clinical uses. Cocaine is applied to produce local anesthesia with intensive vasoconstriction on mucous membranes. It is applied to procedure anesthesia in the nose, throat, ear, and in bronchoscopy (a procedure in which an instrument is used to inspect the bronchi).

(2) Forms available. Cocaine is supplied in the form of a white powder. Cocaine solution must be compounded. It is a Schedule II controlled substance.

4-8. LOCAL ANESTHETICS USED FOR TOPICAL APPLICATION ONLY

a. **Dichlorotetrafluorethane (Freon®)**

(1) Clinical uses. Dichlorotetrafluorethane is a nonflammable and non-explosive agent for topical anesthesia of the skin. It is especially useful for localized minor surgical procedures. This agent should not be sprayed on the skin for a period that exceeds 45 seconds.

(2) Forms available. Dichlorotetrafluorethane is available in a spray form.

b. **Ethyl Chloride**.

(1) Clinical uses. This agent is used for topical anesthesia of the skin.

(2) Forms available. Ethyl chloride is available in a spray form.

Continue with Exercises

EXERCISES, LESSON 4

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which of the following statements best defines the term local infiltration?

   a. A type of anesthesia achieved by applying the anesthetic agent to the surface of mucous membranes to block nerve transmissions.

   b. A type of anesthesia achieved when the nerve endings in the skin and subcutaneous tissues are blocked by direct contact with a local anesthetic that is injected into the tissue.

   c. A type of anesthesia accomplished by injecting a nerve that leads to the operative site.

   d. A type of anesthesia accomplished by injecting a local anesthetic into the peridural space.

2. Which of the following statements best describes the mechanism of action of local anesthetics?

   a. Local anesthetics destroy the nerve tissue so that electrical impulses cannot be carried.

   b. Local anesthetics greatly increase the number of electrical impulses being transmitted so that pain cannot be felt in that particular area.

   c. Local anesthetics block depolarization of the nerve membrane so that the conduction of the nerve impulse is impossible.

   d. Local anesthetics remove both potassium and sodium ions from the nerve tissue so that polarity in the nerve cannot be accomplished; therefore, the impulses are not allowed to move past a certain point in the tissue.

3. Why is hyaluronidase (Wydase®) used in conjunction with local anesthetics?

    a. Hyaluronidase concentrates the local anesthetic in a particular area in order that its effects might be prolonged.

    b. Hyaluronidase neutralizes the local anesthetic so that undesired adverse effects are greatly reduced.

    c. Hyaluronidase is an enzyme that acts to tenderize the tissue and make the nerves more sensitive to the effects of the local anesthetic.

    d. Hyaluronidase increases the movement of the local anesthetic through the tissue.

4. Select the caution(s) and warning(s) associated with the use of local anesthetics.

    a. When a local anesthetic is to be injected, the plunger should be aspirated in several planes to ensure the drug is not being injected into a vein.

    b. Discolored solutions of local anesthetic should be thrown away.

    c. A previously used vial of local anesthetic solution should never be reautoclaved.

    d. All the above.

5. Select the toxicity(ies) associated with the use of local anesthetics.

    a. Large amounts of systemically absorbed local anesthetics can cause depression of the cardiovascular system.

    b. Local anesthetics, even when given in small amounts, cause tremors, shivering, and convulsions.

    c. Local anesthetics cause respiratory depression.

    d. Local anesthetics tend to produce hypersensitive reactions in most people.

SPECIAL INSTRUCTIONS FOR EXERCISES 6 THROUGH 9. Match the trade and generic names of the local anesthetics.

6.	Tetracaine _____	a.	Americaine®
7.	Mepivacaine _____	b.	Freon®
8.	Dichlorotetrafluorethane _____	c.	Pontocaine®
9.	Benzocaine _____	d.	Carbocaine®

10. Select the clinical use of ethyl chloride.

    a. Used to produce anesthesia when applied to the eye.

    b. Used for topical anesthesia of the skin.

    c. Used for infiltration and caudal anesthesia.

    d. Used to produce anesthesia in mucous membranes procedures.

11. What is the clinical use of proparacaine?

    a. Used to produce topical anesthesia on the skin.

    b. Used to produce both anesthesia and vasoconstriction when applied to certain tissues.

    c. Used in nerve block, spinal, and caudal anesthesia.

    d. Used to produce anesthesia in the eye.

12. What is the clinical use of bupivacaine (Marcaine®)?

    a. Used to produce anesthesia when applied to the eye.

    b. Used to produce infiltration, nerve block, and epidural anesthesia.

    c. Used to produce anesthesia when applied to the skin or mucous membranes.

    d. Used to produce anesthesia in a localized area when applied topically (that is, bronchoscopy).

13. Select the caution and warning associated with the use of procaine (Novocaine®).

    a. The drug should not be applied topically.

    b. The drug should not be used for infiltration anesthesia.

    c. The drug should not be used to produce spinal anesthesia.

    d. The drug should not be used to produce nerve block anesthesia.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 4

1. b (para 4-1b)
2. c (para 4-2)
3. d (para 4-4)
4. d (para 4-5b, d, and e)
5. a (para 4-6c)
6. c (para 4-7h)
7. d (para 4-7b)
8. b (para 4-8a)
9. a (para 4-7j)
10. b (para 4-8b)
11. d (para 4-7i)
12. b (para 4-7d)
13. a (para 4-7f)

End of Lesson 4

LESSON ASSIGNMENT

LESSON 5 The Central Nervous System.

TEXT ASSIGNMENT Paragraphs 5-1--5-15.

LESSON OBJECTIVES After completing this lesson, you should be able to:

5-1. Given a list of types of tissue, select the two types of nervous tissues.

5-2. From a list of functions, select the function(s) for which nervous tissues are specialized.

5-3. Given one of the following terms: neuron, dendrite, or axon, and a group of definitions, select the definition of that term.

5-4. Given the shape, diameter, or function of a type of neuron and a list of types of neurons, select the type of neuron described.

5-5. Given a group of statements, select the statement that best describes the neuromuscular junction.

5-6. Given a group of statements, select the statement that best describes the function of a neurotransmitter.

5-7. From a list of chemical substances, select the substance(s) which is/are (a) neurotransmitter(s).

5-8. Given a list of names, select the names of the three major divisions of the human nervous system.

5-9. Given a list of names, select the names of the two major subdivisions of the central nervous system.

5-10. From a list of functions, select the function(s) of the cerebrospinal fluid.

5-11. Given the name of one of the major subdivisions of the human brain and a list of functions, select the function(s) of that part.

5-12. Given a list of functions, select the function of the meninges surrounding the brain and spinal cord.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 5

THE CENTRAL NERVOUS SYSTEM

Section I. BASIC CONCEPTS OF THE NERVOUS SYSTEM

5-1. TYPES OF NERVOUS TISSUES

There are two types of nervous tissues--the neurons (nerve cells) and glia (neuroglia). The neuron is the basic structural unit of the nervous system. The glia are cells of supporting tissue for the nervous system. There are several different types of glia, but their general function is support (physical, nutritive, and so forth.).

5-2. SPECIALIZATION

Nervous tissues are specialized to:

a. Receive stimuli (cells receiving stimuli are said to be "irritable," as are all living cells somewhat).

b. Transmit information.

c. “Store” information.

Section II. THE NEURON AND ITS "CONNECTIONS"

5-3. DEFINITION OF A NEURON

A neuron (figure 5-1) is a nerve cell body and all of its branches.

5-4. TYPES OF NEURON BRANCHES

There are two types of neuron branches--dendrites and axons.

a. **Dendrite.** A dendrite is a neuron process that carries impulses toward the cell body. Each neuron may have one or more dendrites. Dendrites receive information and transmit (carry) it to the cell body.

b. **Axon**. An axon is a neuron branch that transmits information from the cell body to the next unit. Each neuron has only one axon.

c. **Information Transmission**. Information is carried as electrical impulses along the length of the neuron.

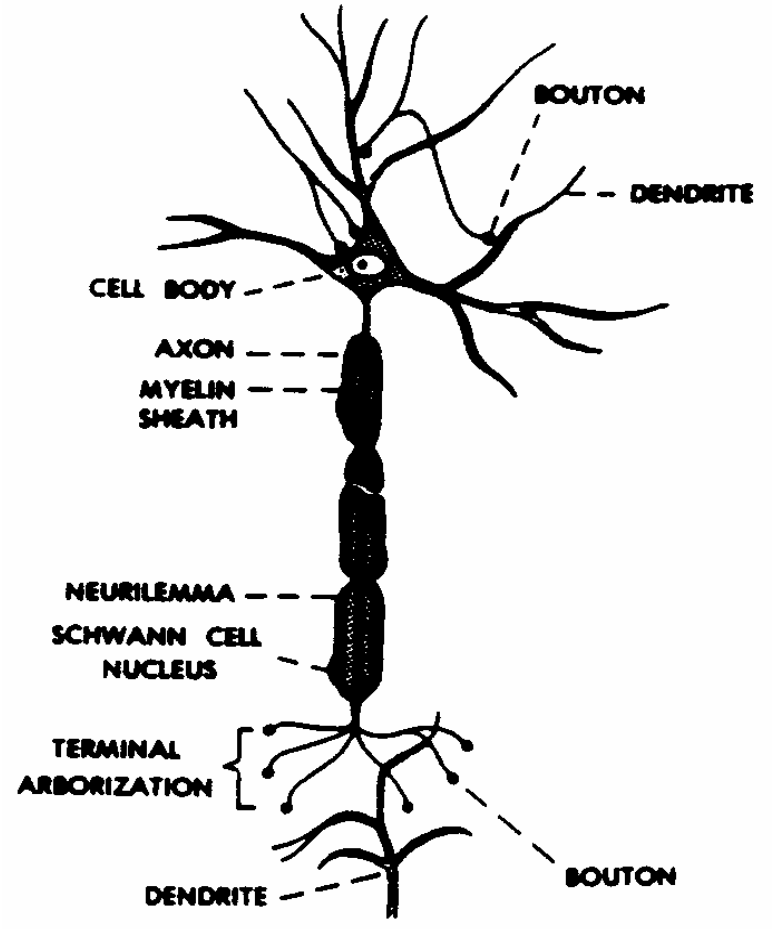


Figure 5-1. A neuron.

d. **Coverings**. Some neuron processes have a covering that is a series of Schwann cells, interrupted by nodes (thin spots). This gives the neuron branch the appearance of links of sausages. The Schwann cells produce a lipid (fatty) material called myelin. This myelin acts as an electrical insulator during the transmission of impulses.

5-5. TYPES OF NEURONS

Neurons may be identified according to shape, diameter of their branches, or function.

a. **According to Shape**. A pole is the point where a neuron branch meets the cell body. To determine the type according to shape, count the number of poles.

(1) Multipolar neurons. Multipolar neurons have more than two poles (one axon and two or more dendrites).

(2) Bipolar neurons. Bipolar neurons have two poles (one axon and one dendrite).

(3) Unipolar neurons. Unipolar neurons have a single process that branches into a T-shape. One arm is an axon; the other is a dendrite.

b. **According to Diameter (Thickness) of Branches**. Neurons may be rated according to the thickness of myelin surrounding the axon. In order of decreasing thickness, they are rated A (thickest), B, and C (thinnest). The thickness affects the rate at which impulses are transmitted. The thickest carry the impulses the fastest. The thinnest carry the impulses the slowest.

c. According to Function.

(1) Sensorv neurons. In sensory neurons, impulses are transmitted from receptor organs (for pain, vision, hearing, and so forth) to the central nervous system (CNS). Sensory neurons are also known as afferent neurons.

(2) Motor neurons. In motor neurons, impulses are transmitted from the central nervous system to muscles and glands (effector organs). Motor neurons may be called efferent neurons.

(3) Interneurons. Interneurons transmit information from one neuron to another. Interneurons connect sensory neurons with motor neurons.

(4) Others. There are other, more specialized types of neurons found in the body (for example, central nervous system).

5-6. NEURON "CONNECTIONS"

A neuron may "connect" either with another neuron or with a muscle fiber. A phrase used to describe such "connections" is "continuity without contact." Neurons do not actually touch. There is just enough space to prevent the electrical transmission from crossing from the first neuron to the next. This space is called the synaptic cleft. Information is transferred across the synaptic cleft by chemicals called neurotransmitters. Neurotransmitters are manufactured and stored on only one side of the cleft. Because of this, information flows in only one direction across the cleft.

a. **The Synapse**. A synapse (figure 5-2) is a “connection” between two neurons.

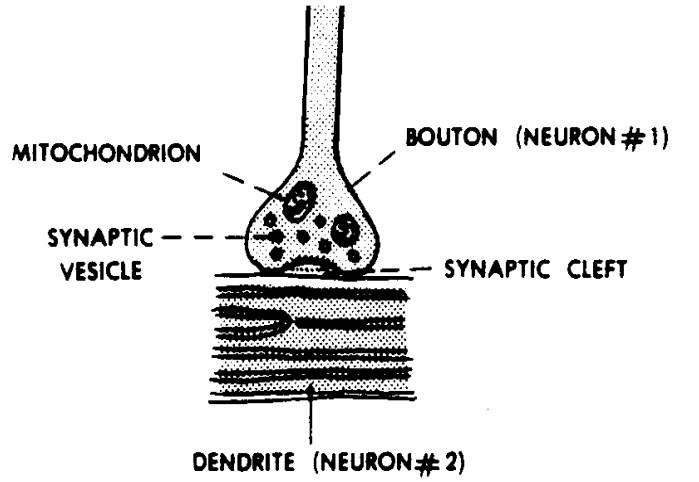


Figure 5-2. A synapse.

(1) First neuron. An axon terminates in tiny branches. At the end of each branch is found a terminal knob. Synaptic vesicles (bundles of neurotransmitters) are located within each terminal knob. That portion of the terminal knob that faces the synaptic cleft is thickened and is called the presynaptic membrane. This is the membrane through that neurotransmitters pass to enter the synaptic cleft.

(2) Synaptic cleft. The synaptic cleft is the space between the terminal knob of the first neuron and the dendrite or cell body of the second neuron.

(3) Second neuron. The terminal knob of the first neuron lies near a site on a dendrite or the cell body of the second neuron. The membrane at this site on the second neuron is known as the postsynaptic membrane. Within the second neuron is a chemical that inactivates the used neurotransmitter.

b. **The Neuromuscular Junction**. A neuromuscular junction (figure 5-3) is a "connection" between the terminal of a motor neuron and a muscle fiber. The neuromuscular junction has an organization identical to a synapse. However, the knob is much larger. The postsynaptic membrane is also larger and has foldings to increase its surface area.

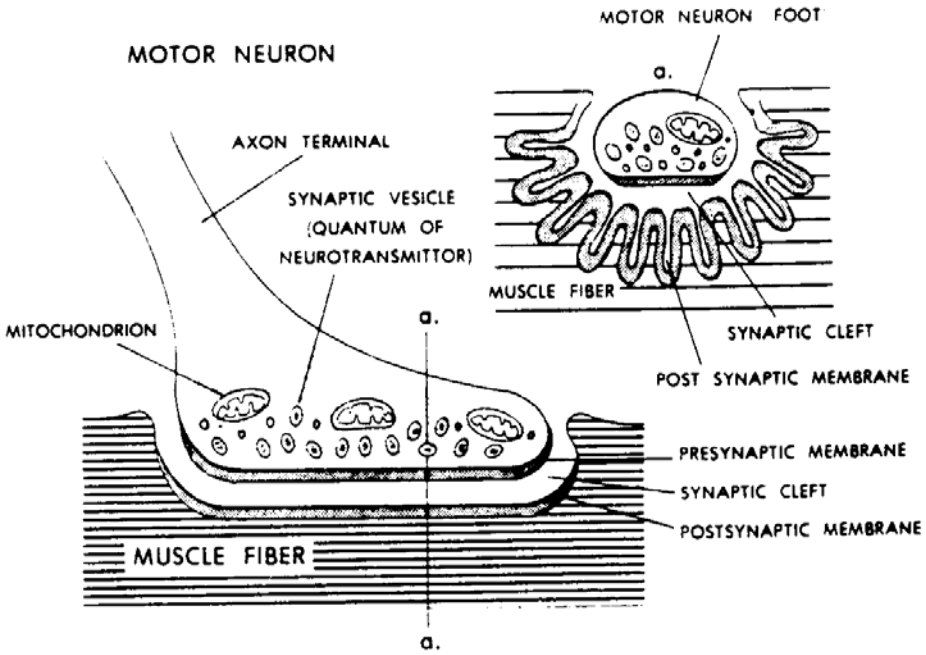


Figure 5-3. A neuromuscular junction.

(1) Motor neuron. The axon of a motor neuron ends as it reaches a skeletal muscle fiber. At this point, it has a terminal konb. Within this konb are synaptic vesicles (bundles of neurotransmitters). The presynaptic membrane lines the surface of the terminal knob and lies close to the muscle fiber.

(2) Synaptic cleft. The synaptic cleft is a space between the terminal knob of the motor neuron and the membrane of the muscle fiber.

(3) Muscle fiber. The terminal knob of the motor neuron protrudes into the surface of the muscle fiber. The membrane lining the synaptic space has foldings and is called the postsynaptic membrane. Beneath the postsynaptic membrane is a chemical that inactivates the used neurotransmitter.

5-7. PROCESS OF NEUROTRANSMISSION

a. The dendrites receive the impulse and transfer it to the nucleus. The nucleus will then cause a change in the permeability of the membrane surrounding the axon. Potassium, which is normally present in high concentrations within the axon, will diffuse out. Sodium, which is usually present in high concentrations outside the axon, will rush into the axon. This exchange of potassium and sodium is called depolarization. As these electrolytes change positions, an electrical charge is set up and the impulses will travel down the axon until it reaches the terminal bulbs. When the impulse reaches the terminal bulbs, it will cause a release of neurotransmitters stored there into the synaptic cleft. Once in the synaptic cleft, the neurotransmitters will diffuse across the synapse to the dendrite of the postsynaptic neuron causing it to depolarize (see figure 5-2).

b. Once the postsynaptic neuron has depolarized, the neurotransmitters must be removed from the synaptic cleft to prevent further depolarization. This is accomplished by two means. The neurotransmitter is either reabsorbed into the terminal bulb or an enzyme destroys it. This process ends the impulse.

c. Before the neuron can depolarize again, the electrolyte sodium and potassium must resume their original positions. The sodium pump theory states that before the neuron can depolarize again the sodium is pumped out and the potassium is pumped back in (repolarized).

5-8. NEUROTRANSMITTERS

A neurotransmitter is a chemical substance that aids in the transmission of an impulse across the synapse. An impulse will cause the release of a neurotransmitter, which is synthesized and stored in terminal bulbs of the axon. The neurotransmitter will diffuse across the synaptic cleft and Initiate an impulse in the postsynaptic nerve. The neurotransmitter reacts with a receptor-site on the postsynaptic nerve initiating an impulse. The neurotransmitter must be removed from the synaptic cleft to stop the impulse.

a. **Acetylcholine.** Acetylcholine (Ach) is destroyed by acetylcholinesterase (AchE) in the synaptic cleft.

b. **Norepinephrine.** Norepinephrine (NE) is removed from the synaptic cleft by:

(1) Reabsorption (reuptake) into the terminal knob.

(2) Destroyed by catechol-o-methyl transferase (COMT).

(3) Destroyed by monoamine oxidase (MAO).

(4) Dilution by diffusion out of the junctional cleft.

5-9. THE ALL OR NONE LAW

This law states that if a stimulus is strong enough to cause a nerve impulse, it will cause the entire fiber to depolarize and not just part of it.

Section III. THE HUMAN CENTRAL NERVOUS SYSTEM

5-10. GENERAL COMMENTS

The human nervous system is divided into three major divisions: the central nervous system (CNS), the autonomic nervous system (ANS), and the peripheral nervous system (PNS). The central nervous system is composed of the brain and spinal cord. Both the peripheral nervous system and the autonomic nervous system carry information to and from the central nervous system. The central nervous system is so named because of its anatomical location along the central axis of the body and because it is central in function. If we use a computer analogy to understand that it is central in function, the CNS would be the central processing unit and the other two parts of the nervous system would supply inputs and transmit outputs. Figure 5-4 shows the central nervous system.

a. **Major Subdivisions of the Central Nervous System.** The major subdivisions of the central nervous system are the brain and spinal cord.

b. **Coverings of the Central Nervous System.** Bone and fibrous tissues cover the parts of the central nervous system. These coverings help to protect the delicate tissue of the CNS.

c. **Cerebrospinal Fluid**. The cerebrospinal fluid (CSF) is a liquid that is thought to serve as a cushion and circulatory vehicle within the central nervous system.

5-11. THE HUMAN BRAIN

The human brain has three major subdivisions: brainstem, cerebellum, and the cerebrum. The central nervous system is first formed as a simple tube like structure in the embryo. The concentration of nervous tissues at one end of the human embryo to produce the brain and head is referred to as cephalization. When the embryo is about four weeks old, it is possible to identify the early forms of the brainstem, cerebellum, and the cerebrum, as well as the spinal cord. As development continues, the brain is located within the cranium in the cranial cavity. See figure 5-5 for illustrations of the adult brain.

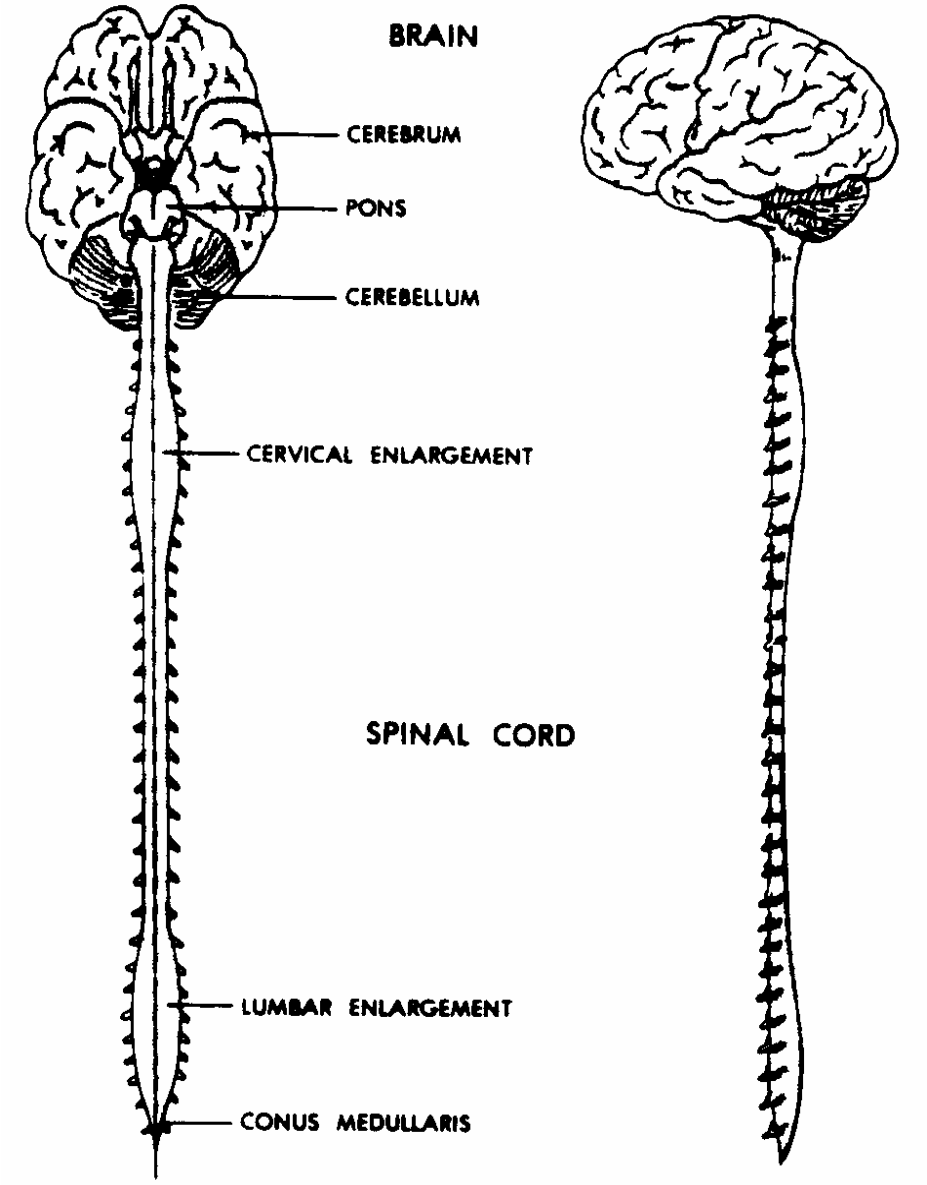


Figure 5-4. The central nervous system (CNS).

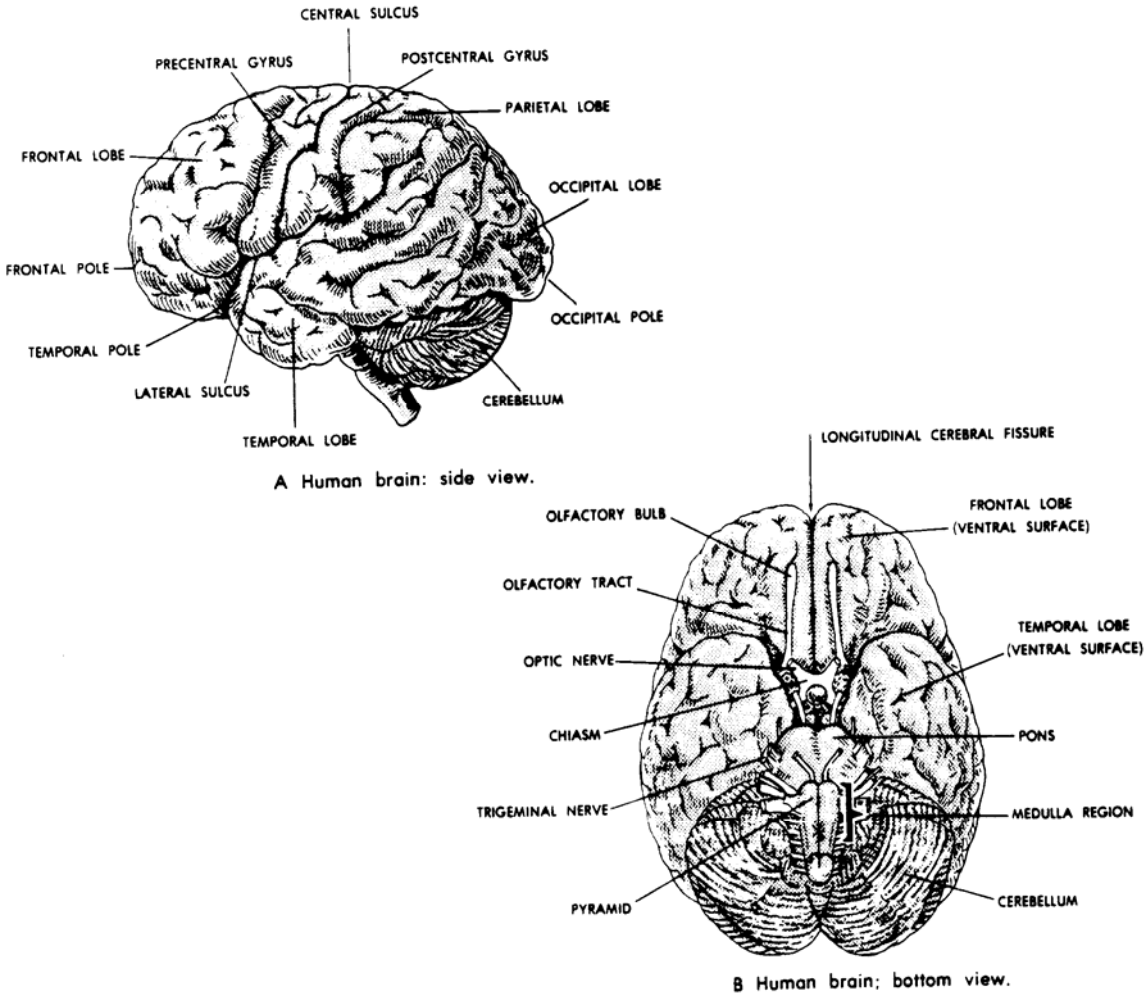


Figure 5-5. Human brain: A side view, B bottom view.

a. **The Brainstem**. The term brainstem refers to that part of the brain that would remain after the removal of the cerebrum and the cerebellum. The brainstem is the basal portion (portion of the base) of the brain. The brainstem can be divided as follows.

FOREBRAINSTEM	thalamus
MIDBRAINSTEM	corpora quadrigemina
HINDBRAINSTEM	pons medulla

(1) The brainstem is continuous with the spinal cord. Together, the brainstem and the spinal cord are sometimes known as the neuraxis.

(2) The brainstem provides major relays and controls for passing information up or down the neuraxis.

(3) The 12 pairs of cranial nerves connect at the sides of the brainstem.

b. **Cerebellum**. The cerebellum is the spherical mass of nervous tissue attached to and covering the hindbrainstem. It has a narrow central part called the vermis and right and left cerebellar hemispheres.

(1) Peduncles. The peduncles is a stemlike connecting part. The cerebellum is connected to the brainstem with three pairs of peduncles.

(2) General shape and construction. A cross section of the cerebellum reveals that the outer cortex is composed of gray matter (cell bodies of neurons), with many folds and sulci (shallow grooves). More centrally located is the white matter (myelinated processes of neurons).

(3) Function. The cerebellum is the primary coordinator/integrator of motor actions of the body.

c. **Cerebrum.** The cerebrum consists of two very much-enlarged hemispheres connected to each other by a special structure called the corpus callosum. Each cerebral hemisphere is connected to the brainstem by a cerebral peduncle. The surface of each cerebral hemisphere is subdivided into areas known as lobes. Each lobe is named according to the cranial bone under which it lies: frontal, parietal, occipital, and temporal.

(1) The cerebral cortex is the gray outer layer of each hemisphere. Deeper within the cerebral hemispheres the tissue is white. The "gray matter" represents cell bodies of neurons. The "white matter" represents the axons.

(2) The areas of the cortex are associated with groups of related functions.

(a) For example, centers of speech and hearing are located along the lateral sulcus, at the side of each hemisphere.

(b) Vision is centered at the rear in the area known as the occipital lobe.

(c) Sensory and motor functions are located along the central sulcus, which separates the frontal and parental lobes of each hemisphere. The motor areas are located along the front side of the central sulcus, in the frontal lobe. The sensory areas are located along the rear side of the central sulcus in the parietal lobe.

d. **Ventricles**. Within the brain, there are interconnected hollow spaces filled with cerebrospinal fluid (CSF). These hollow spaces are known as ventricles. The right and left lateral ventricles are found in the cerebral hemispheres. The third ventricle is located in the forebrainstem. The fourth ventricle is in the hindbrainstem. The fourth ventricle is continuous with the narrow central canal of the spinal cord.

5-12. THE HUMAN SPINAL CORD

a. **Location and Extent**. Referring to figure 5-6, you can see that the typical vertebra has a large opening called the vertebral (or spinal) foramen. Together, these foramina form the vertebral (spinal) canal for the entire vertebral column. The spinal cord, located within the spinal canal, is continuous with the brainstem. The spinal cord travels the length from the foramen magnum at the base of the skull to the junction of the first and second lumbar vertebrae.

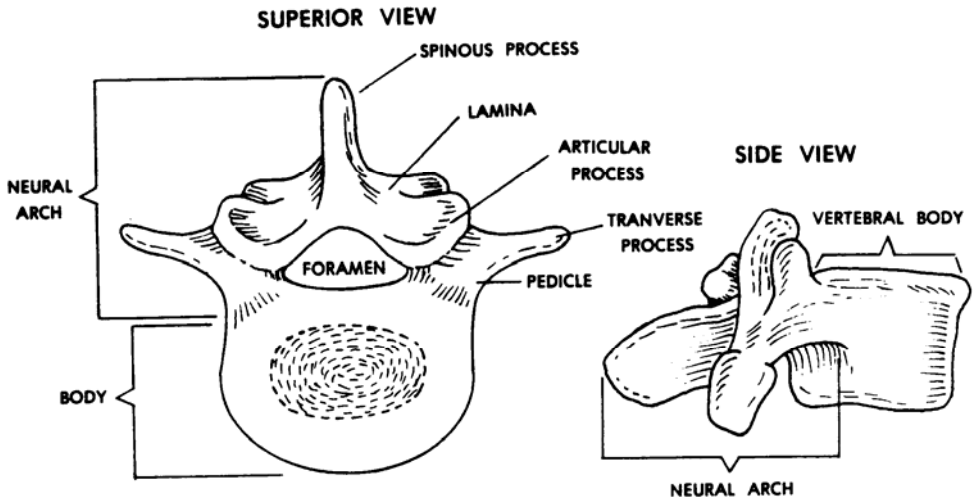


Figure 5-6. The spinal column.

(1) Enlargements. The spinal cord has two enlargements. One is the cervical enlargement, associated with nerves for the upper members. The other is the lumbosacral enlargement, associated with nerves for the lower members.

(2) Spinal nerves. A nerve is a bundle of neuron branches that carry impulses to and from the CNS. Those nerves arising from the spinal cord are spinal nerves. There are 31 pairs of spinal nerves.

b. **A Cross Section of the Spinal Cord**. The spinal cord is a continuous structure that runs through the vertebral canal down to the lumbar region of the column. It is composed of a mass of a central gray matter (cell bodies of neurons) surrounded by peripheral white matter (myelinated branches of neurons). The gray matter and white matter are thus considered columns of material. However, in cross section (figure 5-7), this effect of columns is lost.

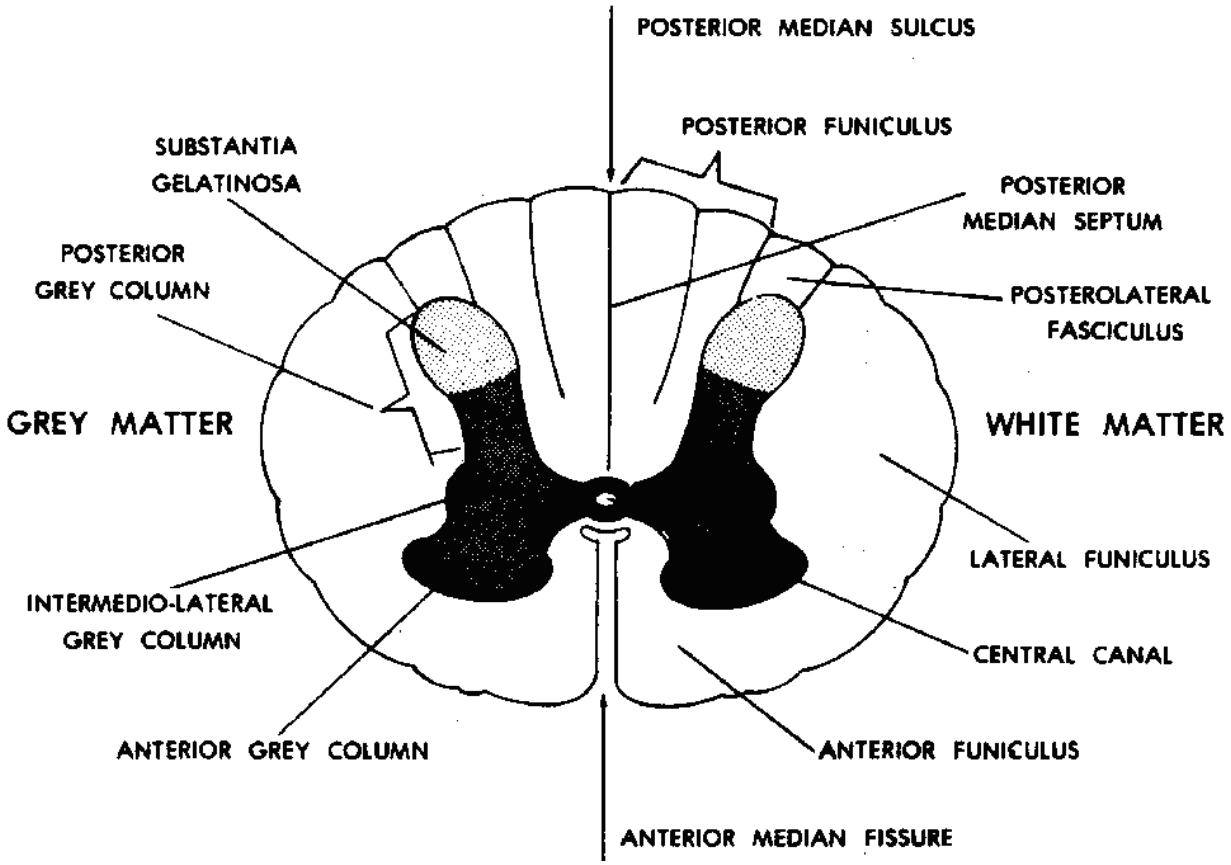


Figure 5-7. A cross section of the spinal cord.

5-13. COVERINGS OF THE CENTRAL NERVOUS SYSTEM

The coverings of the central nervous center (CNS) are skeletal and fibrous.

a. **Skeletal Coverings**.

(1) Brain. The bones of the cranium form a spherical case around the brain. The cranial cavity is the space enclosed by the bones of the cranium.

(2) Spinal cord. The vertebrae, with the vertebral foramina, form a cylindrical case around the spinal cord. The overall skeletal structure is the vertebral column (spine). The vertebral (spinal) canal is the space enclosed by the foramina of the vertebrae.

b. **Meninges (Fibrous Membranes)**. The brain and spinal cord have three different membranes called meninges surrounding them (figure 5-8). These coverings provide protection.

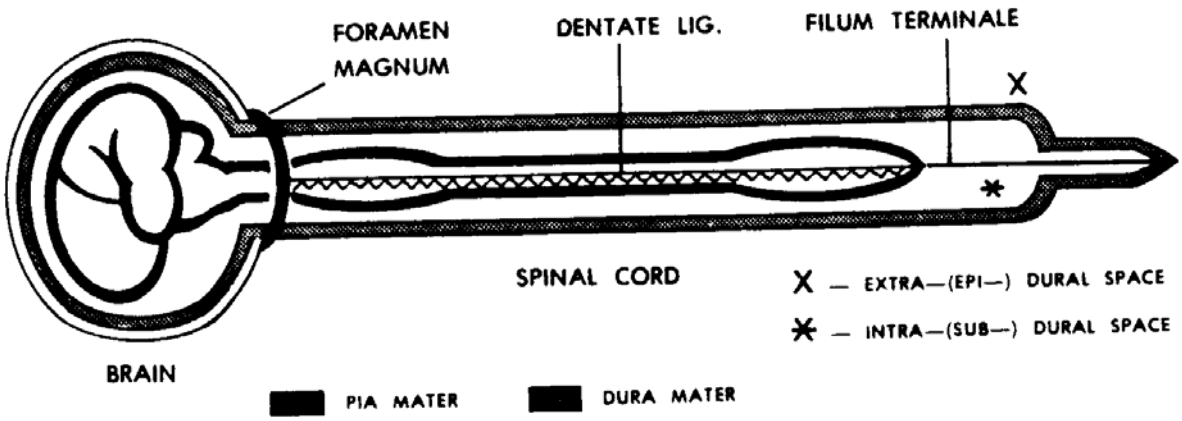


Figure 5-8. The meninges, as seen in side view of the CNS.

(1) Dura mater. The dura mater is a tough outer covering for the CNS. Beneath the dura mater is the subdural space, which contains a thin film of fluid.

(2) Arachnoid mater. To the inner side of the dura mater and subdural space is a fine membranous layer called the arachnoid mater. It has fine spider-web type threads that extend inward through the subarachnoid space to the pia mater. The subarachnoid space is filled with cerebrospinal fluid (CSF).

ARACHNOID = Spiderlike

(3) Pia mater. The pia mater is a delicate membrane applied directly to the surface of the brain and the spinal cord. It carries a network of blood vessels to supply the nervous tissues of the CNS.

5-14. BLOOD SUPPLY TO THE CNS

a. **Blood Supply of the Brain**. The paired internal carotid arteries and the paired vertebral arteries supply blood rich in oxygen to the brain. Branches of these arteries join to form a circle under the base of the brain. This is called the cerebral circle (of Willis). From this circle, numerous branches supply specific areas of the brain.

(1) A single branch is often the only supply to that particular part of the brain. Such an artery is called an end artery. If it fails to supply blood to that specific area, the area will die (as in a stroke).

(2) The veins and venous sinuses of the brain drain into the paired internal jugular veins. These veins carry blood back toward the heart.

b. **Blood Supply of the Spinal Cord**. The blood supply of the spinal cord is by way of combination of three longitudinal arteries running along its length and reinforced by segmental arteries from the sides.

5-15. CEREBROSPINAL FLUID

A clear fluid called cerebrospinal fluid (CSF) is found in the cavities of the central nervous system. Cerebrospinal fluid is found in the ventricles of the brain, the subarachnoid space, and the central canal of the spinal cord. Cerebrospinal fluid and its associated structures make up the circulatory system for the CNS.

a. **Choroid Plexuses**. Choroid plexuses are special collections of arterial capillaries found in the roofs of the third and fourth ventricles of the brain. The choroid plexuses continuously produce CSF from the plasma of the blood.

b. **Path of the Cerebrospinal Fluid Flow**. Blood flows through the arterial capillaries of the choroid plexuses. As the choroid plexuses produce CSF, it flows into all four ventricles. Cerebrospinal fluid from the lateral ventricles flows into the third ventricle, through the cerebral aqueduct then into the fourth ventricle. By passing through three small holes in the roof of the fourth ventricle, CSF enters the subarachnoid space. From the subarachnoid space, the CSF is transported through the arachnoid villi (granulations) into the venous sinuses. Thus, the CSF is formed from arterial blood and returned to the venous blood.

Continue with Exercises

EXERCISES, LESSON 5

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which of the following is/are a type of nervous tissue?

   a. Neurons.

   b. Axons.

   c. Dendrites.

   d. Glia.

2. Select the function(s) for which nervous tissues are specialized.

   a. To transmit information.

   b. To "store" information.

   c. To receive stimuli.

   d. All the above.

3. A neuron is defined as:

   a. A process that carries impulses toward the cell body.

   b. A branch that transmits information from the cell body to the next unit.

   c. A nerve cell body and all of its branches.

   d. A nerve process that has two or more poles.

4. A dendrite is defined as:

    a. A neuron process that carries impulses toward the cell body.

    b. A neuron branch that transmits information from the cell body to the next unit.

    c. A neuron that has two poles.

    d. A nerve cell body and all of its branches.

5. What type of neuron is being described by this statement: "In this type of neuron, impulses are transmitted from the central nervous system to muscles and glands."

    a. Sensory neurons.

    b. Interneurons.

    c. Afferent neurons.

    d. Motor neurons.

6. Which of the following statements best describe the neuromuscular junctions?

    a. A connection between two neurons.

    b. A connection that relays information from muscle tissue to the brain.

    c. A connection between the terminal knob of a motor neuron and a muscle fiber.

    d. A connection which joins two neurons.

7. Which of the following substances is a neurotransmitter?

    a. Sodium chloride.

    b. Norepinephrine.

    c. Acetylcholinesterase.

    d. Catechol-o-methyl transferase (COMT).

8. Select the names of the three major subdivisions of the human nervous system.

   a. The central nervous system, brain, and spinal cord.

   b. The autonomic nervous system, the peripheral nervous system, and the central nervous system.

   c. The peripheral nervous system, the brain, and the spinal cord.

   d. The autonomic nervous system, the peripheral nervous system, and the codaptive nervous system.

9. What is the function of the meninges surrounding the brain and spinal cord?

   a. They carry nervous impulses into the brain and spinal cord.

   b. They prevent nerve impulses from injuring delicate tissue.

   c. They direct nerve impulses to the proper places in the brain.

   d. They provide protection for the brain and spinal cord.

10. What is the function of the cerebrum of the human brain?

    a. It serves as the primary coordinator/integrator of motor actions in the body.

    b. It serves as the center of speech, hearing, and vision.

    c. It provides major relays and controls for passing information up or down the neuraxis.

    d. It protects the cerebellum.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 5

1. a
   d (para 5-1)
2. d (paras 5-2a, b, and c)
3. c (para 5-3)
4. a (para 5-4a)
5. d (para 5-5c(2))
6. c (para 5-6b)
7. b (para 5-8b)
8. b (para 5-10)
9. d (para 5-13b)
10. b (para 5-11c(2))

End of Lesson 5

LESSON ASSIGNMENT

LESSON 6	Agents Used During Surgery.
TEXT ASSIGNMENT	Paragraphs 6-1--6-10.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

6-1. Given a group of definitions, select the definition of the term general anesthetic.

6-2. Given a list, select the types of general anesthetic.

6-3. Given a type of medication used during surgery and a list of drugs, select the drug that belongs to that category of general anesthetics.

6-4. Given the name of an agent used during surgery and a list of uses, side effects, and/or cautions and warnings, select the use, side effect, or caution and warning associated with that agent.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 6

AGENTS USED DURING SURGERY

Section I. GENERAL ANESTHETIC AGENTS

6-1. INTRODUCTION

a. Have you ever undergone surgery? If you have, you can readily appreciate the importance of drugs used during surgery. This group of agents is widely used. The agents within the group differ widely in their uses and indications. This lesson will focus on this group of drugs with the intent of giving you a background in this important area.

b. In days gone by, various substances (that is, whiskey) were used to "put the patient to sleep" during surgery. As surgical procedures became increasingly sophisticated, the need for better anesthetic agents became more apparent. Today, general anesthetic agents comprise an important group of pharmacological agents. Their use promotes patient welfare. This section of the subcourse will discuss this important group of agents.

6-2. DEFINITION

A general anesthetic is an agent that depresses the central nervous system reversibly, producing loss of consciousness, analgesia, and muscle relaxation, with minimal depression of the patient's vital functions. That is, a general anesthetic agent places the patient in a state of anesthesia in which his muscles are relaxed and he feels no pain. Later, after the procedure has been completed, the patient can regain consciousness and recuperate.

6-3. MECHANISM OF ACTION OF GENERAL ANESTHETICS

It is known that the general anesthetic agents depress the central nervous system. Precisely how this depression occurs is unknown. Several theories attempt to explain this depression. One-theory states the agents affect lipid (fat) structures in the brain in order to produce the central nervous system depression. If you desire a detailed discussion of the various theories, you should consult a pharmacology text.

6-4. TYPES OF GENERAL ANESTHETIC AGENTS

There are two broad types of general anesthetics: The inhalation agents and the intravenous agents. It is not the purpose of this subcourse to provide a complete listing or a detailed discussion of the agents that are presented. If you desire additional information on these agents, you should consult a pharmacology text.

a. **Inhalation Agents**. Inhalation anesthetic agents are gases or volatile liquids. These substances are often mixed with oxygen and the patient is allowed to breathe the mixture. After a period, a sufficient level of the anesthetic agent is obtained in the blood and anesthesia is produced. In general, anesthesia can be well controlled with these agents because the concentration of the agent in the blood can be increased or decreased easily by either increasing or decreasing the concentration of the agent in the air the patient is breathing. It is relatively uncommon for a patient to have an allergic reaction to one of the inhalation general anesthetic agents. However, the side effects of some of these agents can be quite serious. There is rapid recovery for the patient when this type of agent is used. That is, when the patient is no longer allowed to breathe the agent, the depression of the central nervous system quickly disappears.

(1) Nitrous oxide. Nitrous oxide is a gas supplied in blue metal cylinders. Nitrous oxide is commonly referred to as laughing gas. Although nitrous oxide is a safe general anesthetic, it is relatively weak in terms of producing anesthesia and muscle relaxation. Consequently, nitrous oxide is often used in conjunction with other agents. Nitrous oxide is often used in dental surgery and in obstetrical practice during delivery.

(2) Halothane (Fluothane®). Halothane is a volatile liquid inhalation anesthetic. It is one of the most widely used general anesthetics. Since halothane does not produce potent analgesia and muscle relaxation, other agents are sometimes administered with halothane on an as-needed basis. Halothane has popularity because it is nonexplosive, rapid acting, pleasant smelling, and is compatible with other drugs.

(3) Enflurane (Erthrane®. Enflurane is a volatile liquid inhalation anesthetic with many of the properties of halothane. It produces greater muscle relaxation than halothane, but like halothane, it is a poor analgesic.

b. **Intravenous Agents**. Intravenous general anesthetics are sterile solutions intended to be administered into the patient's circulatory system. Intravenous anesthetic agents do produce loss of consciousness; however, most of these agents lack the ability to produce complete analgesia. In general, the level of anesthesia is more difficult to control with intravenous anesthetics than with inhalation anesthetics.

(1) Thiopental sodium (Pentothal®) Thiopental sodium is an ultrashort acting barbiturate. That is, this agent acts very quickly to produce anesthesia. Sometimes this agent is used alone for minor surgical procedures. In other cases, the drug is used to initiate anesthesia. Then, other anesthetic agents are used to maintain the anesthesia. Thiopental sodium is a NOTE Q item. That is, it is a controlled substance.

(2) Fentanyl (Sublimaze®) and droperidol (Innovar®). This agent is an intravenously administered product, which combines the narcotic analgesic effect of fentanyl with the sedative and antiemetic effects of droperidol. This agent produces a semiconscious state in the patient, and it is used in types of surgery in which the surgeon needs the cooperation of the patient. Innovar is usually used in combination with nitrous oxide because of its slow induction. Innovar may also be used for various diagnostic procedures. This product is a controlled substance (Note R item).

(3) Ketamine (Ketalar®) is a nonbarbiturate anesthetic that can be administered either intravenously or intramuscularly. Ketamine produces a dissociative type anesthesia in which the patient becomes detached mentally from the environment. Ketamine may be used for induction anesthesia or for diagnostic or minor surgical procedures in children.

Section II. OTHER AGENTS USED DURING SURGERY

6-5. INTRODUCTION

No single anesthetic agent is capable of producing the deep levels of analgesia and skeletal muscle relaxation required during all types of surgery. Consequently, other drugs that have certain desired effects are administered along with the general anesthetic being used. Five major categories of these agents will be presented in this subcourse. They are analgesic agents, drying agents, skeletal muscle relaxants, sedative and hypnotic agents, and antianxiety agents.

6-6. ANALGESIC AGENTS

Analgesic agents relieve pain. Although a general anesthetic agent will produce unconsciousness, the patient might still be able to feel some pain. In these cases, a preanesthetic medication might be administered to the patient in order to relieve the pain. A variety of analgesic agents are available to achieve this purpose. Following are some commonly used agents:

a. Meperidine (Demerol®).

b. Morphine.

c. Nubain®.

d. Stadol®.

6-7. DRYING AGENTS

It is sometimes advantageous during an operation to have the patient's mucous membranes (that is, nose, throat) dry. Drying agents are administered for just this reason. You are probably familiar with the use of drying agents in certain over-the-counter cold medications. Following are two commonly used drying medications:

a. Atropine Sulfate.

b. Glycopyrrolate (Robinul®).

6-8. NEUROMUSCULAR BLOCKING AGENTS

In some types of surgery (for example, abdominal surgery) it is highly advantageous to have the patient's skeletal muscles (for example, abdominal surgery) in a state of relaxation. Most general anesthetic agents do not produce a sufficient level of skeletal muscle relaxation. Therefore, neuromuscular blocking agents are administered to achieve the desired muscle relaxation effects. Two commonly used neuromuscular blocking agents:

a. Vecuronium (Norcuron®).

b. Succinylcholine (Anectine®).

6-9. SEDATIVE AND HYPNOTIC AGENTS

To ensure a good night's sleep prior to a surgical procedure, patients are sometimes administered either a sedative or a hypnotic agent. Agents commonly used for this purpose are:

a. Pentobarbital (Nembutal®).

b. Secobarbital (Seconal®).

6-10. ANTIANXIETY AGENTS

As one might expect, some patients are highly anxious about upcoming surgical procedures. Such increased anxiety interferes with the functioning of the patient (interferes with rest and decreases appetite). Anti-anxiety agents help to control this anxiety. Diazepam (Valium®) is sometimes used to control anxiety.

Continue with Exercises

EXERCISES, LESSON 6

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the definitions below, select the definition of the term general anesthetic.

   a. An agent that depresses the central nervous system irreversibly to produce a loss of consciousness, analgesia) and muscle relaxation.

   b. An agent that stimulates the central nervous system, thus making it possible for a physician to perform various types of surgeries.

   c. An agent used to produce localized analgesia in a patient.

   d. An agent that depresses the central nervous system reversibly to produce a loss of consciousness, analgesia, and muscle relaxation.

2. From the list below, select the type(s) of general anesthetic.

   a. Local.

   b. Intravenous.

   c. Induction.

   d. Clinical.

3. From the list below, select the agent that is classified as an inhalation anesthetic agent.

   a. Thiopental sodium (Pentothal®).

   b. Enflurane (Ethrane®).

   c. Glycopyrrolate (Robinal®).

   d. Succinylcholine (Anectine®).

4. From the list below, select the agent classified as an intravenous anesthetic agent.

    a. Fentanyl (Sublimaze®) and droperidol (Innovar®).

    b. Glycopyrrolate (Robinal®).

    c. Meperidine hydrochloride (Demerol®).

    d. Succinylcholine (Anectine®).

5. From the list of uses below, select the use of glycopyolate (Robinal®)

    a. Intravenous anesthetic agent.

    b. Skeletal muscle relaxant.

    c. Drying agent.

    d. Inhalation anesthetic agent.

6. From the list of uses below, select the use of succinylcholine (Anectine®).

    a. An antianxiety agent used the night before surgery.

    b. A sedative used the day before surgery.

    c. An analgesic agent used after surgery.

    d. A neuromuscular blocking agent used during surgery.

7. From the list of uses below, select the use of meperidine hydrochloride (Demerol®).

    a. An agent often used as a preanesthetic analgesic.

    b. An analgesic used to produce unconsciousness.

    c. An analgesic agent used for its ability to dry the patient's mouth.

    d. An analgesic agent used to stimulate a patient's breathing during surgery.

8. From the list below, select the use of ketamine (Ketalar®).

   a. An inhalation anesthetic used to induce anesthesia for diagnostic purposes.

   b. An intravenous anesthetic used to perform major surgery in adults over the age of 60.

   c. An intravenous anesthetic used to perform minor surgical procedures in children.

   d. An inhalation anesthetic agent used because of its ability to produce analgesia.

9. From the group below, select the use of the agent fentanyl and droperidol (Innovar®).

   a. An agent that is used because it produces a dissociative type of anesthesia.

   b. An agent used because the patient easily inhales it.

   c. An agent used when the surgeon needs the cooperation of the patient because it produces a semiconscious state in the patient.

   d. An agent used during surgery because it produces a drying effect in the patient's mucous membranes.

10. From the group below, select the use of the agent diazepam (Valium®).

    a. A drying agent used to reduce saliva product in comatose patients.

    b. An analgesic agent administered after surgery.

    c. An antianxiety agent used to reduce a patient's apprehension before surgery.

    d. A nonbarbiturate anesthetic used before surgery.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 6

1. d (para 6-2)
2. b (para 6-4b)
3. b (para 6-4a(3))
4. a (para 6-4b(2))
5. c (para 6-7)
6. d (para 6-8)
7. a (para 6-6)
8. c (para 6-4b(3))
9. c (para 6-4b(2))
10. c (para 6-10)

End of Lesson 6

LESSON ASSIGNMENT

LESSON 7 Sedative and Hypnotic Agents.

TEXT ASSIGNMENT Paragraphs 7-1--7-9.

LESSON OBJECTIVES After completing this lesson, you should be able to:

7-1. Given a group of statements, select the best definition of a sedative-hypnotic.

7-2. From a group of statements, select the statement that best describes the mechanism of action of sedative-hypnotics.

7-3. Given a list of possible effects, select the effect(s) produced by sedative-hypnotics.

7-4. Given an effect produced by the sedative-hypnotics and a group of statements, select the statement that best describes that effect.

7-5. From a list of possible clinical uses, select the clinical use(s) of the sedative-hypnotics.

7-6. From a list of adverse reactions, select the adverse effect(s) associated with sedative-hypnotics.

7-7. From a list of cautions and warnings, select the caution(s) and warning(s) associated with the sedative-hypnotics.

7-8. Given a group of statements and two types of barbiturates (for example, ultra short-acting and short-acting), select the statement which best differentiates between the two types.

7-9. Given the trade name of a sedative-hypnotic agent and a list of generic names, match the trade name with its generic name.

7-10. Given the trade or generic name of a sedative-hypnotic agent and a group of possible clinical uses or side effects, select the use(s) or side effect(s) associated with that agent.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 7

SEDATIVE AND HYPNOTIC AGENTS

Section I. BACKGROUND

7-1. INTRODUCTION

Sedative and hypnotic agents form an important class of drugs that are widely used in modern medical practice. The names of many of the agents should be fairly familiar to you since these drugs are so widely used in hospitals and dispensed to patients on an outpatient basis. You probably know that most sedative-hypnotic agents are controlled because of their abuse/misuse potential. The barbiturates have been regarded as the prototypes of this class of drugs because of their extensive use over the past 80 years. Because of their potential for addiction, physical dependence, and side effects, the barbiturates have been replaced by the benzodiazepines (for example, Valium®). The benzodiazepines are currently the most important sedative hypnotics because of their efficacy and safety.

7-2. DEFINITION OF SEDATIVE-HYPNOTIC

A sedative-hypnotic agent is a substance, which, if given in progressively larger doses, produces calm (sedation), sleep (hypnosis), general anesthesia, and ultimately death (because of medullary depression). Sedative-hypnotic agents are commonly used for symptomatic relief of anxiety and for the induction of sleep. Sedatives may be also referred to as anti-anxiety agents.

Section II. CLINICALLY IMPORTANT INFORMATION CONCERNING SEDATIVE-HYPNOTICS

7-3. INTRODUCTION

Sedative-hypnotic agents are an important group of drugs, which are often prescribed to a variety of patients. You should be familiar with the effects and the clinical uses of these drugs.

7-4. THE PHARMACOLOGICAL ACTIONS OF SEDATIVE-HYPNOTIC AGENTS

a. **Mechanism of Action.** Sedatives and hypnotics selectively depress the reticular activating system (RAS), the mechanism responsible for keeping us awake.

b. **Effects Produced by Sedative-Hypnotic Agents.**

(1) Sedation. To sedate means to calm; therefore, sedation refers to the act of producing calm in a patient. You can also think of sedation as referring to a decreased responsiveness to a constant level of stimulation. Small doses (small amounts) of a sedative-hypnotic drug administered to a patient will produce sedation.

(2) Disinhibition. Disinhibition refers to actions a person may perform while under the effects of a drug that he would not perform if he were not taking the drug. This effect may be seen as euphoria, (feeling of well being or elation) in some patients and is a potential source of abuse of these agents. Disinhibition is presumed because of depression of a higher cortical (brain) center, which results in a resultant release of lower brain centers from constant inhibitory influence. Larger doses of a sedative-hypnotic agent will produce this effect.

(3) Relief of anxiety. This particular effect probably cannot be separated from the sedative and euphoriant effects produced by the sedative-hypnotic agents.

(4) Sleep. Sedative-hypnotic induced sleep differs in several ways from normal sleep. If a sufficiently large dose of any sedative-hypnotic agent is administered to a patient, sleep will result; however, the dose of a particular agent required to produce sleep will vary with the physiologic and psychologic state of the individual and the environmental situation in which the drug is given.

(5) Anesthesia. State III of general anesthesia (surgical anesthesia--unconsciousness and paralysis of reflexes) can be induced in humans with large doses of sedative-hypnotic agents. Short- and ultra short-acting barbiturates are the only drugs used as anesthetic agents from this class.

(6) Analgesia. Patients who have been deeply anesthetized with barbiturates are totally unresponsive to pain.

(7) Anticonvulsant activity. All the barbiturates commonly used in clinical practice are capable of inhibiting convulsions. Phenobarbital and other long-acting drugs are selectively more effective at lower therapeutic doses in the treatment of epilepsy.

(8) Cardiovascular and respiratory effects. Sedative-hypnotic agents are respiratory depressants that depress the respiratory system. Sedative-hypnotic agents do not, when administered orally, produce significant cardiovascular effects.

(9) Dependence. Both psychic and physical dependence has been reported with both the barbiturate and nonbarbiturate sedative-hypnotic agents. Dependence usually occurs when sedative-hypnotics are given over a long period in large doses. Therefore, continued administration of these agents is usually necessary to prevent a withdrawal state in the patient.

7-5. CLINICAL USES OF SEDATIVE-HYPNOTIC AGENTS

Sedative-hypnotic agents are used to treat a variety of conditions. These include:

a. **Relief of Anxiety**. Sedative-hypnotics are effectively used to temporarily relieve anxiety associated with threatening or fearful situations (for example, anxiety that typically occurs before a surgical procedure).

b. **Treatment of Depression**. Depression is the most common manifestation of anxiety. Treatment of depression with sedative-hypnotic agents may be effective. It should be noted that major (psychotic) depressions might be intensified with sedative-hypnotics.

c. **Induction of Sleep (Hypnosis)**. Short-acting sedative-hypnotics are generally used because of less hangover or persistent effects. When used to produce sleep, sedative-hypnotics should not be administered continuously and should only be part of an overall plan of management and counseling.

d. **Anticonvulsant Therapy**. Some sedative-hypnotics (for example, phenobarbital) have been successfully used in the treatment of various types of convulsive disorders.

e. **Skeletal Muscle Relaxation**. Some sedative-hypnotics have been used to produce muscle relaxation in patients. However, the effectiveness of sedative-hypnotics for this use may be related more to their sedative properties than to their ability to produce true muscle relaxation.

f. **Anesthesia**. The ultra short-acting barbiturates (for example, thiopental) are used for surgical procedures of short duration.

7-6. ADVERSE EFFECTS OF SEDATIVE-HYPNOTICS

Sedative-hypnotics, although safe when taken as directed, are not without their side effects. You should be familiar with the side effects produced by these agents:

a. **Drowsiness**. As you might anticipate, all of the sedative-hypnotic agents will cause drowsiness if a large enough dose is given to the patient. Furthermore, because of individual reactions to drugs, some patients will be made drowsy even by small doses of these agents. Patients who are prescribed sedative-hypnotics should be told not to drink alcoholic beverages while taking the drug since the alcohol could intensify the drowsiness effect.

b. **Impaired Performance and Judgment.** These agents interfere with a person 5 ability to think and to perform certain "hands-on" tasks. Sedative-hypnotic agents are equivalent to alcohol in their effects on distorting judgment and minor motor skills.

c. **Hangover Effect**. When a patient arises from a night's sleep after having taken a bedtime dose of a sedative-hypnotic, the patient may complain of feeling dizzy, lethargic, or exhausted. This is referred to as the "hangover effect." This effect is more prevalent with the long-acting sedative-hypnotics.

d. **Chronic Toxicity**.

(1) Drug abuse. The relief of anxiety and the euphoria provided by these drugs has led to the compulsive misuse of every member of this group. Because of their rapid onset of action and intense effect, the short-or intermediate-acting sedative-hypnotics are more apt to be misused than are the other types of sedative-hypnotics. These agents do not cause chronic organic toxicity.

(2) Withdrawal state. A patient who has been taking therapeutic doses of a sedative-hypnotic may find that he has a disturbed pattern of sleep with restlessness and nightmares when he suddenly stops taking the drug. Discontinuing larger doses of sedative-hypnotics may produce a hyperexcitable state in the patient characterized by weakness, tremor, anxiety, elevated blood pressure, and elevated pulse rate. The sudden withdrawal of even larger doses may produce convulsions or toxic psychosis with agitation, confusion, and hallucinations.

e. **Acute Toxicity**. The amount of a particular sedative-hypnotic required to produce death in a patient depends upon a variety of factors. An extremely large dose of a sedative-hypnotic will produce a state of prolonged, deep anesthesia. If the stage of severe medullary depression is reached, circulatory shock occurs. In case of acute toxicity, it is necessary for the patient to be immediately taken to the nearest medical treatment facility for emergency treatment.

7-7. CAUTIONS AND WARNINGS ASSOCIATED WITH THE USE OF SEDATIVE-HYPNOTICS

a. Ambulatory patients (those patients able to walk) should be warned to avoid activities that require mental alertness, judgment, and physical coordination while taking sedative-hypnotics.

b. Alcohol should not be consumed with sedative-hypnotic agents. This is because both the alcohol and the sedative-hypnotic would both act to depress the central nervous system.

c. Caution should be observed when these drugs are given to patients who have impaired liver function, since the sedative-hypnotics are broken down in the liver.

d. Sedative-hypnotic agents are probably best prescribed and taken only on an irregular basis when needed. Some physicians believe that a short (that is, week long) course of scheduled sedative-hypnotic therapy is the most desirable. The aim is not to offer the patient the opportunity to become physically or psychologically dependent upon the drugs.

Section III. CLASSIFICATION OF SEDATIVE-HYPNOTIC AGENTS

NOTE: The agents in this section are classified according to their duration of action and whether they are barbiturates or nonbarbiturates.

7-8. BARBITURATE SEDATIVES AND HYPNOTICS

a. **Ultra Short-Acting Barbiturates.**

(1) Basic information. Ultra short-acting barbiturates usually have a duration of action of 15 to 30 minutes. They are administered intravenously in order to induce anesthesia because of their high degree in lipid (fatty) materials. Ultra short-acting barbiturates are used to counteract the convulsions associated with some chemical substances (for example, tetanus toxin) or by the overdosage of certain drugs.

(2) Examples of ultra short-acting barbiturates.

(a) Methohexital (Brevital®).

(b) Thiopental (Pentothal®).

b. **Short-Acting Barbiturates.**

(1) Basic information. Short-acting barbiturates usually have a duration of action that lasts from 2 hours to 4 hours. Short-acting barbiturates are effective treatment--when taken by mouth--for the initial and short-term treatment of insomnia. These agents are widely used intramuscularly (IM) for preanesthetic sedation in order to calm the patient and to reduce anxiety often found in patients about to undergo surgery. Pentobarbital and secobarbital (see below) may be used for short-term daytime sedation in patients who suffer from anxiety.

(2) Examples of short-acting barbiturates.

(a) Pentobarbital (Nembutal®).

(b) Secobarbital (Seconal®).

c. **Intermediate-Acting Barbiturates**.

(1) Basic information. Intermediate-acting barbiturates have a duration of action that lasts from 4 hours to 6 hours. These agents are mainly use for the initial and short-term treatment of insomnia.

(2) Example of intermediate-acting barbiturate. Amobarbital (Amytal®).

d. **Long-Acting Barbiturates.**

(1) Basic information**.** Long-acting barbiturates have a duration of action that lasts from 6 hours to 8 hours. These agents are used orally to maintain daylong sedation in anxiety-tension states. Furthermore, long-acting barbiturates are useful in the treatment of various convulsive disorders.

(2) Examples of long-acting barbiturates.

(a) Phenobarbital.

(b) Mephobarbital (Mebaral®).

7-9. NON-BARBITURATE SEDATIVES AND HYPNOTICS

a. **Short-Acting Agents.**

(1) Background information. Short-acting non-barbiturate sedative-hypnotics are generally used orally in the initial and short-term treatment of insomnia.

(2) Examples of short-acting non-barbiturate sedative-hypnotics.

(a) Chloral hydrate (Noctec®). Drug interactions may occur between chloral hydrate and anticoagulants, furosemide, alcohol, or other drugs that are CNS depressants.

(b) Triazolam (Halcion®). Triazolam is rapidly absorbed through the oral route and is as effective as the barbiturates in inducing sleep. It is excreted in breast milk and should not be administered to nursing mothers.

b. **Intermediate-Acting Agents**.

(1) Background information. Intermediate-acting non-barbiturate agents are administered orally to effectively control moderate to severe daytime anxiety and tension in patients who have neuroses and mild depressive states.

(2) Examples of intermediate-acting nonbarbiturates.

(a) Diazepam (Valium®). Diazepam may be useful in the treatment of alcohol withdrawal symptoms (for example, delirium tremens, agitation, and so forth.) This agent produces skeletal muscle relaxant effects in humans and has been used with limited success in various neurologic and musculoskeletal disorders. Diazepam may be administered parenterally as a preanesthetic medication to reduce anxiety and to calm the patient. Diazepam is also administered intravenously in the treatment of status

epilepticus. It is available in tablet form (2, 5, and 10 milligrams) and in injection form (5 milligrams per milliliter in 2 and 10 milliliter containers). Diazepam is a Note Q controlled substance in the military.

(b) Meprobamate (Equanil®, Miltown®). Meprobamate can produce skeletal muscle relaxant effects in humans; therefore, it has been used with some success in the treatment of various neurologic and musculoskeletal disorders. It appears to be less effective than diazepam in the treatment of anxiety and tension. The most common side effect associated with the agent is drowsiness. It is supplied in tablet and suspension forms. Meprobamate is a Note Q controlled item in the military.

(c) Other examples of nonbarbiturate used in the treatment of anxiety disorders include Lorazepam (Ativan®), Alprazolam (Xanax®), and Buspirone (Buspar®). Lorazepam is used primarily as an antianxiety agent, but is useful for treating insomnia due to stress and anxiety. Lorazepam is also used as a preanesthetic medication to produce sedation and decrease the patient's ability to recall events related to the day of surgery.

(d) Temazepam (Restoril®). Temazepam is administered in a nightly dose of 15 to 30 mg. It is an effective inducer of sleep with a good safety profile. Animal studies indicate a potential for Temazepam to cause teratogenic effects. Therefore, it should not be administered during pregnancy.

c. **Long-Acting Non-Barbiturate Agents.**

(1) Background information. These agents depress the central nervous system. Patients taking these drugs should be cautioned against performing hazardous activities while under their effects.

(2) Examples of long-acting non-barbiturate agents.

(a) Chlordiazepoxide hydrochloride (Librium®). Chlordiazepoxide is orally administered as an antianxiety agent. It is also effective when administered parenterally in the treatment of alcohol withdrawal. Side effects associated with the agent include drowsiness, ataxia, and lethargy.

(b) Oxazepam (Serax®). Oxazepam is generally less effective than either diazepam or chlordiazepoxide in the treatment of tension and anxiety. Drowsiness is the most common side effect associated with this agent.

Continue with Exercises

EXERCISES, LESSON 7

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which statement best describes the mechanism of action of sedative-hypnotics?

   a. They inhibit the flow of potassium and sodium ions across the semipermeable membranes of the nerves.

   b. They inhibit the depolarization of the nerve fibers and thus produce calm or sleep.

   c. They depress the reticular activating system (RAS).

   d. They inhibit the transmission of electrical impulses from the brain by interfering with the passage of certain ions through the nerve fibers.

2. Select the effect(s) produced by the sedative-hypnotics.

   a. Relief of anxiety.

   b. Disinhibition.

   c. Analgesia.

   d. All the above.

3. Which of the following statements best describes the analgesia produced by sedative-hypnotics?

    a. Patients who have been given extremely large doses of barbiturates are unresponsive to pain.

    b. Patients who are administered intravenous doses of sedative-hypnotics are unable to feel any painful stimuli.

    c. Patients who are given sedative-hypnotics seem to be more tolerant of pain than those patients who are not given these drugs.

    d. Patients who are given any amount of sedative-hypnotics are unable to feel pain, but they are also unable to maintain consciousness for long periods.

4. Select the clinical use(s) associated with the sedative-hypnotics.

    a. To induce sleep.

    b. To treat minimal brain dysfunction (MBD).

    c. To treat pain.

    d. All the above.

5. Select the adverse effect(s) associated with the use of sedative-hypnotic agents.

    a. Drowsiness.

    b. Hangover.

    c. Impaired judgment.

    d. All the above.

6. Select the caution(s) and warning(s) associated with the use of sedative-hypnotics.

    a. Caution should be observed when giving these drugs to patients who have impaired liver function.

    b. These agents should not be prescribed to those persons who are likely to become dependent upon them.

    c. Sedative-hypnotics should be taken on a continuous and regular basis to ensure desired therapeutic effects.

    d. All the above.

SPECIAL INSTRUCTIONS FOR EXERCISES 7 THROUGH 10: Match the generic name of the drug with its corresponding trade name.

7.	Pentobarbital	_____	a. Librium®
8.	Oxazepam	_____	b. Nembutal®
9.	Chlordiazepoxide	_____	c. Serax®
10.	Triazolam	_____	d. Halcion®

11. Select the clinical use(s) of diazepam (Valium®).

    a. A treatment for minimal brain dysfunction (MBD).

    b. An anoretic for the suppression of appetite.

    c. A preanesthetic medication used to calm the patient.

    d. A drug used for induction of sleep.

12. Select the clinical use(s) of chlordiazepoxide.

    a. Antianxiety agent.

    b. Sleep inducer.

    c. Skeletal muscle constrictor.

    d. All the above.

13. What is the most common side effect associated with oxazepam (Serax®)?

    a. Ataxia.

    b. Lethargy.

    c. Drowsiness.

    d. Blurred vision.

14. What is the duration of action for ultra-short acting barbiturates?

    a. 6 to 8 hours.

    b. 4 to 6 hours.

    c. 2 to 4 hours.

    d. 15 to 30 minutes.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 7

1. c (para 7-4a)
2. d (para 7-4b(2), (3), and (4))
3. a (para 7-4b(6))
4. a (para 7-5a)
5. d (para 7-6)
6. a (para 7-7c)
7. b (para 7-8b(2))
8. c (para 7-9c(2)(c))
9. a (para 7-9c(2)(b))
10. d (para 7-9c(2)(a))
11. c (para 7-9b(2)(b))
12. a (para 7-9b(2)(a))
13. c (para 7-9c(2)(c))
14. d (para 7-8a(1))

End of Lesson 7

LESSON ASSIGNMENT

LESSON 8 Anticonvulsant Agents.

TEXT ASSIGNMENT Paragraphs 8-1--8-5.

LESSON OBJECTIVES After completing this lesson, you should be able to:

8-1. Given a group of statements, select the meaning of epilepsy or convulsions.

8-2. Given a group of statements, select the statement that best differentiates between clonic and tonic convulsions.

8-3. Give the name of a type of epilepsy and a group of descriptions, select the best description of that type of epilepsy.

8-4. From a group of potential causes, select the cause(s) of epilepsy in either a child or an adult.

8-5. Given a group of statements, select the statement that best describes the mechanism of action for anticonvulsants.

8-6. Given the trade name of an anticonvulsant agent and a group of generic names, match the trade name with its generic name.

8-7. Given a trade or generic name of an anticonvulsant agent and a group of statements, select the statement that best describes the clinical use(s) or adverse reaction(s) associated with that agent.

8-8. Given a trade or generic name of a convulsant agent, a description of a situation involving the dispensing of that agent, and a group of statements describing cautions and/or warnings to the patient, select the statement that should be made to the patient receiving that medication.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 8

ANTICONVULSANT AGENTS

Section I. REVIEW OF EPILEPSY

8-1. BASIC DEFINITIONS

Before studying about anticonvulsants, you should review/study the definitions that relate to the topic:

a. **Epilepsy**. Epilepsy is a chronic convulsive disorder of cerebral function. Epilepsy is characterized by recurrent attacks of motor, sensory, psychic, or autonomic nature. The attacks may involve changes in the state of patient consciousness and are usually sudden in onset and brief.

b. **Convulsion**. A convulsion is a violent involuntary contraction or series of contractions of the voluntary muscles. There are two types of convulsions.

(1) Clonic convulsions. A clonic convulsion has alternating periods of contraction and relaxation of the voluntary muslce.

(2) Tonic convulsions. A tonic convulsion is a state of sustained contraction of voluntary muscles.

8-2. TYPES OF EPILEPSY

There are four types of epilepsy. Certain signs and symptoms characterize each type.

a. **Grand Mal.** Grand Mal is the most common type of epilepsy. In this type of epilepsy, the person often experiences an aura (this can consist of certain sounds, fear discomfort) immediately before a seizure. Then the patient loss consciousness and has tonic-clonic convulsions. The seizures generally last from 2 to 5 minutes.

b. **Petit Mal**. This type of epilepsy is most frequently found in children. Brief periods of blank spells or loss of speech characterizes petit mal. During the seizures, which usually last from 1 to 30 seconds, the person stops what he is doing and after the seizure resumes what he was doing before the seizure. Many persons are not aware that they have had a seizure.

c. **Jacksonian (Focal).** This type of epilepsy is rare. It is usually associated with an organic lesion of a certain part of the brain (cerebral cortex). Jacksonian epilepsy is characterized by focal or local clonic type convulsions of localized muscle groups (for example, thumb, big toe, and so forth). The seizures normally last from 1 to 2 minutes.

d. **Psychomotor.** Psychomotor epilepsy is rare. Psychomotor epilepsy is characterized by periods of abnormal types of behavior (for example, extensive chewing or swallowing). The localized seizures may advance to generalized convulsions with resultant loss of consciousness.

8-3. CAUSES OF EPILEPSY

a. **In Children.** Epilepsy that occurs in infancy usually results from developmental defects, metabolic diseases, or injuries sustained during birth.

b. **In Adults.** Epilepsy that begins in adulthood usually is caused by trauma (an accident), cerebrovascular accident (a "stroke"), tumors, or diseases associated with the brain.

Section II. ANTICONVULSANT THERAPY

8-4. MECHANISM OF ACTION OF ANTICONVULSANTS

The mode and the site of action anticonvulsants are not known for sure. However, it is believed that the anticonvulsants suppress seizures by depressing the cerebral (motor) cortex of the brain, thereby raising the threshold of the central nervous system (CNS) to convulsive stimuli. Therefore, the person is less likely to undergo seizures.

8-5. SPECIFIC ANTICONVULSANT DRUGS

a. **Phenobarbital.**

(1) Clinical uses. Phenobarbital is orally administered in the treatment of grand mal epilepsy. It is less effective in the treatment of petit mal and psychomotor epilepsy. The injectable from of the drug is used to treat other types of convulsions.

(2) Adverse effects. The most common adverse effects associated with phenobarbital are related to sedation and disinhibition (see lesson 7 of this subcourse). These include dizziness, drowsiness, ataxia (lack of muscular coordination), and nystagmus (a rapid involuntary movement of the eyeball). Furthermore, as discussed in lesson 7 of this subcourse, persons taking phenobarital can experience withdrawal symptoms when they suddenly stop taking the drug. Epileptic patients are unusually susceptible to the hyperexcitable state induced by too rapid reduction of dosage or too rapid withdrawal of phenobarbital.

(3) Cautions and warnings. Patients who take phenobarbital should be warned about drowsiness. Patients who take phenobarbital should not drink alcohol while taking phenobarbital. Dosage of the drug should be reduced by small amounts in order to avoid hastening convulsions. Lastly, phenobarbital may stimulate the activity of a number of enzyme systems and affect the metabolism of various drugs (for example, anticoagulants, phenytoin).

b. **Phenytoin (Dilantin®).**

(1) Clinical uses. Phenytoin is used alone or in combination with phenobarbital in the treatment of grand mal and psychomotor epilepsy. It is also used in the treatment of other types of convulsions.

(2) Adverse effects. Adverse effects associated with phenytoin include ataxia (lack of muscular coordination, staggering walk), nystagmus (a rapid, involuntary movement of the eyeball), and slurred speech. Drowsiness and fatigue may accompany these adverse effects in some patients by tremors and nervousness and in others.

(3) Caution and warning. Drug interactions can occur between phenytoin and alcohol, barbiturates, folic acid, coumarin-type anticoagulants, disulfirams, the sulfonamides, and sympathomimetic agents. Phenytoin should be used cautiously with patients who are alcoholics or who have blood dyscrasias.

c. **Ethosuximide (Zarontin®).**

(1) Clinic use. Ethosuxamide is the drug of first choice for the treatment of petit mal epilepsy.

(2) Adverse effects. Drowsiness, ataxia, and gastrointestinal irritation are adverse effects associated with the use of ethosuxamide.

(3) Caution and warning. Ethosuxamide should be used cautiously with patients who have blood dyscrasias or liver or kidney impairment.

d. **Clonazepam (Klonopin®).**

(1) Clinical uses. Clonazepam is used in the treatment of grand mal epilepsy. It is the alternate drug for the treatment of petit mal in patients who fail to respond to ethosuxamide (Zarontin) therapy.

(2) Adverse effects. The primary side effect associated with clonazepam is central nervous system depression. Drowsiness is frequently seen in patients who take this medication.

e. **Diazepam (Valium®), Lorazepam (Ativan®)**.

(1) Clinical uses. Diazepam or Lorazepam are drugs of first choice for the treatment of status epilepticus (a particular type of convulsive disorder) when it is given intravenously.

(2) Adverse effects. Drowsiness, fatigue, and ataxia are the most common adverse effects seen with diazepam.

NOTE: Midazolam (Versed®) may be used as a continuous infusion for the treatment of status epilepticus in patients that fail diazepam or lorazepam.

Continue with Exercises

EXERCISES, LESSON 8

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which of the following statements best describes epilepsy?

   a. A mental condition that can be transmitted from one person to another.

   b. A chronic convulsive disorder of brain function.

   c. A chronic mental condition that is always characterized by violent contractions of the involuntary muscles.

   d. A condition that harms the brain in such a way that the person cannot live a normal life.

2. Which of the following statements best describes grand mal epilepsy?

   a. A type of epilepsy characterized by brief periods of blank spells or loss speech.

   b. A type of epilepsy characterized by focal or local clonic type convulsions of localized muscle groups (for example, thumb, big toe, and so forth).

   c. A type of epilepsy characterized by seizures which generally last from 2 to 5 minutes.

   d. A rare type of epilepsy characterized by periods of abnormal behavior (for example, extensive chewing).

3. Which of the following cause epilepsy in adults?

   a. Tumors.

   b. Trauma.

   c. Cerebrovascular accident.

   d. All the above.

4. The anticonvulsants act by _____.

   a. Depressing the cerebral cortex of the brain, thereby lowering the threshold of the CNS to convulsive stimuli.

   b. Stimulating the cerebral cortex of the brain, thereby raising the threshold of the CNS to convulsive stimuli.

   c. Depressing the cerebral cortex of the brain, thereby raising the threshold of the CNS to convulsive stimuli.

   d. Depressing the cerebral cortex of the brain, thereby deadening the part of the brain that is responsible for the seizures.

SPECIAL INSTRUCTIONS FOR EXERCISES 5 THROUGH 8.: Match the generic name with its corresponding trade name.

5.	Clonazepam _____	a.	Zarontin®
6.	Diazepam _____	b.	Klonopin®
7.	Phenytoin _____	c.	Valium®
8.	Ethosuximide _____	d.	Dilantin®

9. Phenobarbital is orally administered in the treatment of _____.

   a. Grand mal epilepsy.

   b. Petit mal epilepsy.

   c. Jackson epilepsy.

   d. Psychomotor epilepsy.

10. Patients who take phenobarbital should be cautioned not to:

   a. Take aspirin with the drug.

   b. Take the drug with meals.

   c. Take the medication immediately after a seizure.

   d. Take the medication with alcohol.

11. Which adverse effect(s) is/are associated with the use of ethosuximide?

   a. Dizziness.

   b. Ataxia.

   c. Nystagmus.

   d. All the above.

12. Which adverse effect(s) is/are associated with the use of phenytoin.

   a. Nystagmus.

   b. Ataxia.

   c. Slurred speech.

   d. All the above.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 8

1. b (para 8-1a)
2. c (para 8-2a)
3. d (para 8-3b)
4. c (para 8-4)
5. b (para 8-5d)
6. c (para 8-5c)
7. d (para 8-5b)
8. a (para 8-5c)
9. a (para 8-5a)
10. d (para 8-5a(3))
11. b (para 8-5c(2))
12. d (para 8-5b(2))

End of Lesson 8

LESSON ASSIGNMENT

LESSON 9 Psychotherapeutic Agents.

TEXT ASSIGNMENT Paragraphs 9-1--9-20.

LESSON OBJECTIVES After completing this lesson, you should be able to:

9-1. Given a group of statements and one of the four classes of functional mental disorders, select the best description of that class of mental disorders.

9-2. From a group of statements, select the statement that best differentiates between fear and anxiety.

9-3. Given one of the following terms: fear, anxiety, antianxiety agent, depression, antidepressant, antipsychotic agent, or tranquilizer and a group of definitions, select the correct definition of that term.

9-4. Given one of the following categories of drugs: antianxiety agents, antidepressant agents, and antipsychotic agents and a group of statements that describe uses, advantages, disadvantages, adverse effects, or precautions and warnings select the statement that best describes the use(s) advantage(s), disadvantage(s), adverse effect(s), or caution(s) and warning(s) associated with that category of drug.

9-5. Given a group of statements, select the statement that best describes the advantages of antianxiety agents over drugs that were previously used to calm or sedate patients.

9-6. Given the generic and/or trade name of a psychotherapeutic agent and a group of uses, adverse effects, or cautions and warnings, select the use(s), adverse effects, or cautions and warnings associated with that agent.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 9

PSYCHOTHERAPEUTIC AGENTS

Section I. OVERVIEW

9-1. INTRODUCTION

Stress, anxiety, and depression are frequently used words in today's world. Every living person has problems of one type or another. Some people seem to cope quite well with stress most of the time, while other persons need assistance to make adjustments to life. The wise use of psychotherapeutic agents has become an integral part of assisting others to adjust to certain situations. Of course, psychologists and psychiatrists combine other treatment means with the wise use of drugs in their efforts to help others.

9-2. THE FOUR MAJOR CLASSES OF FUNCTIONAL MENTAL DISORDERS

Later in this lesson, certain drugs and their uses will be discussed. In order for you to understand the use of some of the drugs, you must be aware of the four major classes of functional mental disorders.

NOTE: Reality testing is an ego function that consists of an individual's ability to recognize and interpret the surrounding world (that is, what's going on?). The ability to recognize and interpret the surrounding world allows an individual to meet the demands of life and make survival judgments.

a. **Neuroses (Neurotic Disorders)**. Neuroses are a group of conditions characterized by the development of anxiety because of unresolved unconscious conflicts. The neurotic person is anxious, but he does not know the cause of his anxiety. These conditions tend to become chronic. Reality testing is maintained. That Is, the neurotic remains in touch with reality.

b. **Psychoses (Psychotic Disorders).** Psychoses are a group of disorders with more or less severe disturbances of thought, mood, and/or behavior. Psychoses are usually chronic, but short episodes of psychosis do sometimes occur. Reality testing is always lost in one or more important respects. That is, a psychotic is not entirely in touch with his environment.

c. **Personality Disorders.** Personality disorders are types of mental disorders characterized by lifelong maladaptive patterns of adjustment to life. These types of disorders tend to be chronic. Personality disorders are usually recognized by adolescence. Reality testing is usually preserved.

d. **Transient Situational Disturbances (Adjustment Disorders).** Transient situational disturbances (TSD) are temporary emotional disorders of any severity, which occur as reactions to overwhelming environmental stress. Reality testing may or may not be impaired during the acute phase of these disorders.

9-3. TERMINOLOGY ASSOCIATED WITH PSYCHOTHERAPEUTIC AGENTS

Before discussing the various psychotherapeutic agents, some terms and their definitions will be presented. These terms will be used later in the discussion of the psychotherapeutic agents.

a. **Fear**. Fear is a feeling of apprehension caused by a real object in the environment. For example, a person who is unexpectedly confronted with a rattlesnake would probably display fear of the snake. If you closely observed such a surprised person, you would see such signs as increased blood pressure, increased respiratory rate, and increased heart rate. These physiological responses are mediated by the sympathetic nervous system.

b. **Anxiety**. Anxiety is a feeling of apprehension that has no specific object. Most people have experienced the feeling of anxiety that occurs during test-taking time. Anxiety has both positive and negative components. On the positive side, anxiety motivates you to study for the exam rather than to go to the movies. On the negative side, anxiety can interfere with performance on the examination (that is, "black outs" during a pencil and paper test). Interestingly enough, a person who is frightened (that is, with a snake) or is anxious (as with a test) will display the same body signs such as increased blood pressure, increased heart rate, and increased respiratory rate.

c. **Antianxiety Agent.** An antianxiety agent is a drug that is used to calm a patient. Although the drug reduces the subjective feeling of anxiety, it will have no effect on the cause of the anxiety.

d. **Depression**. Depression is a disturbance of mood manifested by decreased self-esteem, decreased vitality, and increased sadness.

e. **Antidepressant**. An antidepressant is a drug that will, after a period, cause an improvement in a depressed patient’s mood.

f. **Antipsychotic Agent.** An antipsychotic agent is a drug that will reduce specific symptoms (that is, hallucinations, delusions) in patients experiencing a psychosis.

g. **Tranquilizer**. The term tranquilizer refers to a wide-variety of drugs that produce a calming change in patient attitude and behavior. At one time, these drugs were categorized into two major categories: the major tranquilizers and the minor tranquilizers. The major tranquilizers are now generally referred to as antipsychotic agents and the minor tranquilizers are referred to as antianxiety agents.

Section II. ANTIANXIETY AGENTS

9-4. INTRODUCTION TO ANTIANXIETY AGENTS

It is not unusual for a person to experience stress and anxiety. Most people can deal with the minor stresses of life without using antianxiety agents. However, when the degree of anxiety increases to the point of causing social and/or economic impairment, the attending physician may decide to prescribe an antianxiety agent. It should be remembered that the antianxiety agent will calm the patient, but the drug cannot remove the cause of anxiety. Often the antianxiety therapy is combined with counseling or therapy to help the patient deal with the stress and anxiety.

9-5. INDICATIONS FOR ANTIANXIETY AGENTS

Antianxiety agents are indicated in patients to control moderate to severe degrees of anxiety. Antianxiety agents are also extremely useful in treating patients when periods of overwhelming stress occur.

9-6. USES OF ANTIANXIETY AGENTS

Antianxiety agents are used in a variety of situations. Listed below are some of those situations.

a. **Control Moderate to Severe Stress and Anxiety in Neurotic and Depressed Patients**. Some neurotic and depressed patients are prescribed antianxiety agents to reduce the amount of subjective anxiety; thus enabling them to more productively participate in counseling or therapy.

b. **Control Stress and Anxiety in Previously Normal Persons in Periods of Overwhelming Stress**. In most cases, normal individuals are able to cope with the stress and anxiety of life. However, when unusual circumstances of extreme stress arise, physicians sometimes prescribe antianxiety agents to assist people during these periods. Antianxiety agents should not be prescribed for dealing with the stresses of everyday life (Food and Drug Administration ruling).

c. **Treat Withdrawal Symptoms in Alcoholism.** These agents are very effective in the treatment of delirium tremens associated with the withdrawal of alcohol from alcoholics.

d. **Treat Psychotic Patients in Periods of Acute Agitation.** Sometimes patients who have certain psychotic conditions undergo periods of acute agitation. Antianxiety agents are used to calm these types of patients during these periods. Thus, the patients become much more manageable. Generally speaking, antipsychotic drugs are more effective when used for this particular purpose.

e. **Decrease Preoperative and Postoperative Apprehension**. Patients who will undergo or have undergone surgery frequently have periods of apprehension. Antianxiety agents have been used to reduce this type of stress and tension.

9-7. ADVANTAGES OF THE USE OF ANTIANXIETY AGENTS

Anti-anxiety agents have two main advantages over drugs that were previously used to calm or sedate patients:

a. **Antianxiety Agents Do Not Cause Excessive Loss of Alertness**. Barbiturates were frequently used to calm patients. Unfortunately, the barbiturates sometimes calmed the patients to an undesirable degree. Although the antianxiety agents produce some degree of sedation during the initial days of therapy, this sedation is usually short-lived.

b. **Overdosage of Antianxiety Agents Rarely Results in Death to the Patient**. As previously stated, the barbiturates were previously used to calm patients. Unfortunately, overdose of barbiturates can frequently result in coma, respiratory depression, and death. Antianxiety agents, on the other hand, are somewhat safe in terms of the amount of drug required to produce coma, respiratory depression, and death. This factor makes the wise use of antianxiety agents in special circumstances useful in the treatment of extremely anxious patients who are entertaining thoughts about suicide.

9-8. DISADVANTAGES OF THE USE OF ANTIANXIETY AGENTS

Although the antianxiety agents do have many advantages over previously used drugs, they are not free from potentially harmful effects. The discussion below focuses on two major disadvantages of the group of drugs classified as antianxiety agents.

a. **Drowsiness.** Antianxiety agents, especially during the first few days of therapy, produce drowsiness in many patients. Further, many patients who take antianxiety drugs experience loss of judgment and a loss of mental powers. Consequently, patients who are on antianxiety therapy should be cautioned not to operate machinery.

b. **Drug Interaction Effects**. The antianxiety agents can interact with central nervous system depressants to produce a further degree of depression to the central nervous system. Thus, patients who are on antianxiety therapy should be cautioned against drinking alcohol or taking other central nervous system depressants.

9-9. EXAMPLES OF ANTIANXIETY AGENTS

This area of the subcourse is designed to provide you with a brief overview of some commonly prescribed antianxiety agents. If you desire further information about the agents discussed below, you should consult a reference (for example, AMA Drug Evaluations) which is well written and easy to understand.

a. **Chlordiazepoxide Hydrochloride (Librium®).**

(1) Uses. Chlordiazepoxide hydrochloride is widely used as an antianxiety agent to help people deal with stress. Further, it is used preoperatively to reduce patient apprehension. As an antianxiety agent, it has less anticonvulsant activity, and it produces less drowsiness than diazepam, another antianxiety drug.

(2) Adverse effects. Chlordiazepoxide is likely to produce such adverse effects as drowsiness and lethargy. These adverse effects are more likely to occur in older patients.

(3) Cautions and warnings. Patients taking chlordiazepoxide should be cautioned not to take a central nervous system depressant like alcohol since the additive effect might produce depression of the central nervous system. Furthermore, patients taking chlordiazepoxide should be cautioned against operating machinery (for example, driving an automobile).

b. **Diazepam (Valium®).**

(1) Uses. Diazepam is widely used for the treatment of anxiety and tension. Further, it is used in the treatment of muscle spasms.

(2) Adverse effects. Diazepam produces such adverse effects as drowsiness, fatigue, and ataxia (lack of coordination). Physical dependence can develop over a period with resultant withdrawal symptoms to include seizures.

(3) Cautions and warnings. An individual taking diazepam should be cautioned against taking central nervous system depressants (that is, alcohol) and operating machinery.

c. **Lorazepam (Ativan®).**

(1) Uses. Lorazepam is primarily used in the treatment of anxiety.

(2) Adverse effects. Lorazepam produces such adverse effects as drowsiness, fatigue, and ataxia (lack of coordination). Physical dependence can develop over a period of time with resultant withdrawal symptoms to include seizures.

(3) Cautions and warnings. An individual taking lorazepam should be cautioned against taking central nervous system depressants (that is, alcohol) and operating machinery.

d. **Alprazolam (Xanax®).**

(1) Uses. Alprazolam is primarily used in the treatment of anxiety and has been useful in the management of panic attacks.

(2) Adverse effects. Alprazoam produces such adverse effects as drowsiness, fatigue, and ataxia (lack of coordination). Physical dependence can develop over a period with resultant withdrawal symptoms to include seizures.

(3) Cautions and warnings. An individual taking alprazolam should be cautioned against taking central nervous system depressants (that is, alcohol) and operating machinery.

e. **Hydroxyzine Hydrochloride (Atarax®) or Hydroxyzine Pamoate (Vistaril®).**

(1) Uses. Hydroxyzine has the following three primary uses:

(a) Antianxiety agent. The drug is used to treat anxiety, tension, and agitation.

(b) Antiemetic agent. Because hydroxyzine does have some antiemetic (antinausea and vomiting) properties, it is used in its injectable form (hydroxyzine pamoate (Vistaril®) to manage postoperative nausea and vomiting.

(c) Antipruritic agent. Hydroxyzine has been used because of its antipruritic (anti-itch) properties.

NOTE: Atarax® is sometimes used as a sedative.

(2) Adverse effects. There is an extremely low incidence of adverse reactions with this drug. Some drowsiness may occur during the initial days of therapy; however, this drowsiness is short-lived.

(3) Cautions and warnings. An individual taking hydroxyzine should be cautioned against drinking alcohol and taking other central nervous system depressants because of the additive effect that may be produced. Furthermore, persons taking this drug should be cautioned against operating machinery (for example, driving an automobile).

f. **Buspirone (Buspar®).**

(1) Uses. Buspirone is used in the management of anxiety or the short term relief of symptoms of anxiety. It is unrelated to the benzodiazepines and therefore lacks the sedative and addictive properties of these agents.

(2) Adverse effects. The most common adverse effects include dizziness, nausea, and headache.

(3) Cautions and warnings. Although buspirone does not produce significant drowsiness, patients should be cautioned about driving or operating machinery until they are certain that this drug does not affect them adversely.

NOTE: Antidepressants which are discussed in the next section are becoming the agents of choice for anxiety disorders.

Section III. ANTIDEPRESSANT AGENTS

9-10. INTRODUCTION TO ANTIDEPRESSANT AGENTS

Depression is a frequently occurring psychiatric disorder. Patients with medical and surgical conditions frequently have signs and symptoms associated with depression. People who are depressed usually have low moods, decreased physical activity and mental alertness, decreased appetite, abnormal sleep patterns, and morbid preoccupations. Depression can be of rapid or slow onset. For example, a soldier who has been denied leave might display several signs of depression. This type of depression could be of rapid onset.

9-11. INDICATIONS FOR ANTIDEPRESSANT AGENTS

a. Most people undergo changes in mood. You can probably remember when you have been "up" (that is, right before a three-day weekend) and when you have been "down" (that is, right after a three-day weekend). Physicians have found antidepressant agents to be useful in the treatment of depression, which is not time limited and causes the patient social and economic difficulties.

b. Depression can be caused by chemical imbalances in the body, by stress, and by situations in the environment. It has been found that psychotherapy, reduction of stress, and improvement in the environment can be successful in treating some types of depression. However, in depression that results from chemical imbalances in the body, these types of treatment have not proven to be very effective.

9-12. EFFECTS OF ANTIDEPRESSANT AGENTS

Antidepressant agents elevate mood, increase physical activity and mental alertness, improve appetite and sleep patterns, and reduce morbid preoccupations. These effects are not seen immediately upon beginning antidepressant therapy. Instead, one to four weeks may pass before the patient shows any signs of improvement in the depression. This period is called the therapeutic lag period.

9-13. PRECAUTIONS ASSOCIATED WITH THE USE OF ANTIDEPRESSANT AGENTS

Although the antidepressant agents are safe for patient use, there are some precautions associated with their use:

a. Antidepressants should be used cautiously with patients who are hyperactive or agitated.

b. Antidepressants should be used cautiously with the elderly, with patients who have glaucoma, and with patients who have hypertension (high blood pressure).

c. Antidepressants may interact with other types of drugs. For example, references should be consulted to determine if any interaction could occur between a particular antidepressant and a drug a patient is taking to control high blood pressure, since some antidepressants partially block the action of some antihypertensive drugs. In addition, the action of some drugs (that is, the barbiturates) is increased in duration when they are administered to patients who are taking certain antidepressant agents.

9-14. SPECIFIC ANTIDEPRESSANT AGENTS

Immediately following is a discussion of several antidepressant agents. By no means is the listing below complete in terms of the number of agents available to the physician. Further, no attempt has been made to provide an in-depth discussion of each individual agent. If you desire additional information about any of the agents discussed below, you should consult a pharmacology reference (for example, AMA Drug Evaluations).

a. **Fluoxetine (Prozac®).**

(1) Uses. Fluoxetine belongs to a class of antidepressants called Selective Serotonin Reuptake Inhibitors (SSRIs). SSRIs are usually regarded as the treatment of choice for depression due to less side effects and a better safety profile than older agents. Fluoxetine is used to treat depression and anxiety disorders. The Serafem® product is approved for premenstrual dysphoric disorder (PMDD).

(2) Adverse effects. Fluoxetine may produce the following adverse effects:

(a) Miscellaneous effects (that is, sexual dysfunction).

(b) Central nervous system effects (for example, agitation and insomnia).

(c) Gastrointestinal effects (that is, nausea and diarrhea).

(3) Cautions and warnings.

(a) Do not overlap with other anti-depressants or monoamine oxidase inhibitors.

(b) The drug may produce drowsiness.

(c) The patient should not consume any alcohol while taking the drug.

NOTE: Other SSRIs include Sertraline (Zoloft®), Paroxetine (Paxil®), Citalopram (Celexa®), and Fluvoxamine (Luvox®).

b. **Imipramine Hydrochloride (Tofranil®).**

(1) Uses. Imipramine is used to treat depression; however, it can paradoxically aggravate the anxiety sometimes associated with depression. Imipramine also produces an anticholinergic effect and is therefore approved by the Food and Drug Administration (FDA) for the treatment of enuresis (bedwetting) in children.

(2) Adverse effects. Imipramine may produce the following adverse effects:

(a) Cardiovascular effects (that is, orthostatic hypotension).

(b) Central nervous system effects (for example, confusion and anxiety).

(c) Gastrointestinal effects (that is, nausea and vomiting).

(d) Anticholinergic effects (for example, dry mouth and constipation).

(3) Cautions and warnings.

(a) Abruptly taking the drug away from the patient after long-term therapy may produce withdrawal symptoms.

(b) The drug may produce drowsiness.

(c) The patient should not consume any alcohol while taking the drug.

(d) The drug should be used with caution in patients with glaucoma or urinary retention because of its anticholinergic effects.

c. **Desipramine (Norpramin®).**

(1) Uses. Desipramine is used to treat depression. It has also been used in facilitating withdrawal from cocaine.

(2) Adverse effects. Desipramine is closely related to imipramine but has only minimal cardiovascular, CNS, GI, and anticholinergic effects.

(3) Cautions and warnings.

(a) Abruptly taking the drug away from the patient after long-term therapy may produce withdrawal symptoms.

(b) The drug may produce drowsiness.

(c) The patient should not consume any alcohol while taking the drug.

(d) The drug should be used with caution in patients with glaucoma or urinary retention because of its anticholinergic effects.

d. **Amitriptyline Hydrochloride (Elavil®).**

(1) Uses. Amitriptyline is used in the treatment of depression and neuropathic pain syndromes.

(2) Adverse effects. Amitriptyline tends to cause confusion in elderly patients. In addition, it has other adverse effects that are similar to those produced by imipramine hydrochloride.

(3) Cautions and warnings.

(a) Abruptly taking the drug away from the patient after long-term therapy may produce withdrawal symptoms.

(b) The drug may produce drowsiness.

(c) The patient should not consume any alcohol while taking the drug.

(d) The drug should be used with caution in patients who have glaucoma or urinary retention due to its anticholinergic effects.

(4) Precautions. Amitriptyline can be cardiotoxic to some individuals.

d. **Nortriptyline Hydrochloride (Aventyl®).**

(1) Uses. Nortriptyline is used in the treatment of depression and neuropathic pain disorders.

(2) Adverse effects. The adverse effects produced by nortriptyline are the same as those produced by imipramine hydrochloride (see para 9-14b).

(3) Cautions and warnings. The adverse effects produced by nortriptyline are the same as those produced by imipramine hydrochloride (see para 9-14b).

e. **Trazodone (Desyrel®).**

(1) Uses. Trazodone is used in the treatment of depression. It is unrelated to any of the antidepressants discussed thus far.

(2) Adverse effects. The adverse effects produced by Trazodone include skin rash, chest pain, drowsiness, tachycardia, vivid dreams/nightmares, and muscle aches.

(3) Cautions and warnings. Trazodone may produce drowsiness and may cause irregular heartbeat. The patient should observe caution when driving or performing other tasks requiring alertness. Alcohol and other depressant drugs should be avoided while taking Trazodone.

f. **Nefazodone Hydrochloride (Serzone®)**.

(1) Uses. Nefazodone hydrochloride is an oral antidepressant that is totally unrelated to the other available antidepressants.

(2) Adverse effects. The adverse effects of Nefazodone hydrochloride are similar to selective serotonin reuptake inhibitors.

(3) Contraindications.

(a) The drug is contraindicated in patients who are taking other monoamine oxidase (MAO) inhibitors, and those having hypersensitivity to Nefazodone or other phenylpiperazine antidepressants.

(b) The drug is contraindicated on patients who are taking nonsedating antihistimines (that is, Terfenadine and Astemizole).

(4) Cautions and warnings. Patients taking Nefazodone hydrocloride should be cautioned against the following:

(a) The drug may produce drowsiness.

(b) The patient should not consume any alcohol while taking the drug.

(c) Patients with cardiovascular or cerebrovascular disease that could be exacerbated by hypotension should use with caution.

(d) The potential for a fatal outcome is significantly increased by the concurrent use of alprazolam and triazolam.

Section IV. ANTIPSYCHOTIC AGENTS

9-15. INTRODUCTION TO ANTIPSYCHOTIC AGENTS

The general term psychoses encompass a wide variety of conditions. Each specific condition has particular signs and/or symptoms that assist the psychiatrist in making a diagnosis. Some psychotic conditions require long-term hospitalization, while others can be managed on an outpatient basis. Many psychotic patients show marked disorganization of thought patterns and behavior with either increased or decreased psychomotor activity. Antipsychotic agents help psychotic patients better organize their thoughts and coordinate their motor activities. In some cases, the use of antipsychotic agents can mean the difference between hospitalization and home-care.

9-16. INDICATIONS FOR USE OF ANTIPSYCHOTIC AGENTS

In order for an antipsychotic agent to be wisely used to treat a psychotic patient, the attending psychiatrist must carefully examine the patient and diagnose the specific condition. Proper diagnosis is the key word for beginning drug therapy for the psychotic patient.

9-17. USES OF ANTIPSYCHOTIC AGENTS

a. The antipsychotic agents are used to treat various conditions of psychosis. When used in this manner, they help reduce the patient's fear, panic, and hostility. With this help, the patient is better able to organize life and more realistically respond to the environment.

b. Some antipsychotic agents are used as adjuncts in anesthesia to control nausea and vomiting.

c. The state of psychotic hyperarousal is the first group of symptoms to respond to antipsychotic medication. Delusions and hallucinations resolve more gradually over a period.

9-18. ADVERSE EFFECTS ASSOCIATED WITH ANTIPSYCHOTIC AGENTS

As with most drugs, the antipsychotic agents produce some adverse effects. Discussed below are some of those reactions:

a. **Extrapyramidal Reactions**. Extrapyramidal reactions are manifested by a parkinson-like syndrome. That is, the patient has tremors, muscular rigidity, postural abnormalities, pill-rolling movements with the fingers, and hypersalivation. Fortunately, these symptoms may be relieved or lessened, or the reactions may be prevented before they occur by the administration of diphenhydramine (Benadryl).

b. **Drowsiness, Dizziness, and Fatigue**. Although a sedative-effect is produced by many of the antipsychotic agents, this effect is short-lived because tolerance develops after one to three days.

c. **Orthostatic Hypotension.** Orthostatic hypotension (low blood pressure) is an adverse reaction produced by some of the antipsychotic agents. Patients experiencing this problem are at risk of fainting and injuring themselves.

9-19. DOSAGE PRINCIPLE ASSOCIATED WITH THE ANTIPSYCHOTIC AGENTS

You should be familiar with a dosage principle associated with the antipsychotic agents. This principle is: "High dosage-low potency/low dosage-high potency."

a. **High Dosage/Low Potency.** Initially when treating a psychotic patient, a psychiatrist might choose to select a drug that can be given in a high dosage (large amount of drug) because of its low potency. This allows the psychiatrist some freedom in dosage-especially if the patient is uncontrollable--without potential harm to the patient. High dosage/low potency drugs usually have a high incidence of anti-cholinergic side effects, but low incidence of extrapyramidal side effects.

b. **Low Dosage/High Potency.** After a patient has been on one antipsychotic agent and has been stabilized, the psychiatrist may choose to use another agent that can be given in smaller amounts (low dosage) because of its high potency. Usually, more potent drugs are easier to administer (that is, in tablet form). Low dosage/high potency drugs usually have a low incidence of anti-cholinergic side effects, but high incidence of extrapyramidal side effects

9-20. SPECIFIC ANTIPSYCHOTIC AGENTS

a. **Chlorpromazine (Thorazine®).**

(1) Uses. Chlorpromazine is a phenothiazine drug (a particular class of drugs) used in the treatment of acute and chronic psychoses. It is also used as a pre- or postoperative agent in the prevention of nausea and vomiting.

(2) Adverse effects. Chlorpromazine produces three major adverse effects:

(a) Extrapyramidal reactions. These reactions are frequently seen in both young and elderly patients who are taking large doses of the drug.

(b) Drowsiness.

(c) Orthostatic hypotension. Orthostatic hypotension is most likely to occur when the patient has been administered the drug intravenously. This can be prevented by having the patient remain reclined for at least one hour after the administration of the drug.

(d) Dryness of the mouth.

(3) Cautions and warnings. Chlorpromazine should not be prescribed to patients who have liver disease or glaucoma. Furthermore, patients taking the drug should be cautioned not to drink alcoholic beverages.

b. **Fluphenazine Hydrochloride (Prolixin®, Permitil®).**

(1) Use. Fluphenazine hydrochloride is used in the treatment of psychotic disorders.

(2) Adverse effects.

(a) Extrapyramidal reactions.

(b) Drowsiness or lethargy.

(c) Hypertension (increased blood pressure).

(3) Cautions and warnings. Abrupt withdrawal of the drug may result in nausea and vomiting, gastritis, and dizziness.

c. **Thioridazine Hydrochloride (Mellaril®).**

(1) Use. This is a phenothiazine used to treat acute and chronic types of psychosis. Thioridazine is safe in treating psychotic patients who also have liver disease.

(2) Adverse effects. Thioridazine produces the following adverse effects:

(a) Sedation and lethargy.

(b) Gastric irritation.

d. **Perphenazine (Trilafon®).**

(1) Uses. Perphenazine is used in the management of psychotic disorders.

(2) Adverse effects. Perphenazine, like chlorpromazine, can produce extrapyramidal reactions, orthostatic hypotension, drowsiness, and dry mouth (drowsiness and orthostatic hypotension are less than that seen with chlorpromazine).

(3) Cautions and warnings. Perphenazine may cause drowsiness. Patients should avoid alcohol and other CNS depressants while taking this drug.

e. **Trifluoperazine Hydrochloride (Stelazine®).**

(1) Use. This phenothiazine is used in the treatment of various types of acute and chronic psychoses. This drug is used primarily in the maintenance treatment of psychotic patients.

(2) Adverse effects. Two adverse effects are produced by this drug:

(a) Drowsiness may occur with the use of this drug.

(b) Extrapyramidal reactions may occur with the use of this drug.

(3) Cautions and warnings. The following cautions and warnings are associated with trifluoperazine:

(a) The use of alcohol with this agent should be avoided because of the possible interaction between the two substances.

(b) Since the drug can produce sedation, the patient should be cautioned against operating vehicles while under the effects of this drug.

f. **Haloperidol (Haldol®).**

(1) Use. This drug is used in the treatment of acute and chronic psychosis. In its parenteral (injectable) form (10 milligrams per milliliter of solution), haloperidol is a potent antipsychotic medication which is well suited for emergency room use. Haloperidol can be safely prescribed to patients who have liver disease.

NOTE: Haloperidol is considered the gold standard for antipsychotics.

(2) Adverse effects. Two adverse effects are seen with this drug:

(a) Extrapyramidal reactions.

(b) Depression, anxiety, and/or dizziness.

g. **Lithium Carbonate (Eskalith®, Lithane®).**

(1) Use. Lithium carbonate is used in the treatment of manic-depressive psychosis. After initial administration, approximately 7 to 10 days are required before the effects of the drug can be observed in the patient.

(2) Adverse effects. The following are some of the adverse effects associated with lithium carbonate:

NOTE: The level of lithium carbonate in the bloodstream of the patient is very significant. The severity of the toxic symptoms tends to increase as the level of the drug in the patient's blood increases.

(a) Nausea, vomiting, cramps diarrhea.

(b) Drowsiness and muscular weakness.

(c) Tremors.

(d) Height loss or weight gain.

(3) Cautions and warnings. Cautions and warnings associated with the use of this agent are:

(a) Patients who are administered lithium carbonate should be kept under close medical supervision at all times. This is necessary because the amount of drug required to produce the desired effects is very close to the amount of drug that will produce toxic effects.

(b) Blood levels of lithium carbonate should always be performed at regular intervals to ensure that the appropriate therapeutic levels of the drug are maintained.

(c) Lithium carbonate should not be administered to patients who are taking diuretics (that is, some antihypertensive medications), because diuretics tend to cause an accumulation of the drug, and toxic levels of the drug could rapidly occur.

(d) The efficacy (clinical effectiveness) of lithium carbonate in the treatment of the depressive phase of manic depressive illness remains controversial. The drug is the most effective treatment for true bipolar illness, particularly in the control of manic episodes. The drug is not effective in established depressed episodes. It may prevent reoccurrence of both manic and depressive episodes.

(e) Drowsiness. Patients taking the drug should be cautioned against operating heavy machinery (for example, driving an automobile).

h. **Risperidone (Risperdal®).**

(1) Use. This drug belongs to the class of antipsychotics called “atypical”. They are used for treatment resistance in older agents and reduce the likelihood of extrapyramidal side effects. They may be used as first line agents.

(2) Adverse effects. Adverse effects are seen with this drug:

(a) Extrapyramidal reactions.

(b) Orthostatic hypotension.

NOTE: Other atypical antipsychotics include Olazapine (Zyprexa®), Clozapine (Clozaril®), and Quetiapine (Seroquel®).

Continue with Exercises

EXERCISES, LESSON 9

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the best description of personality disorders.

   a. Types of conditions characterized by the development of anxiety because of unresolved unconscious conflicts.

   b. Temporary emotional disorders that occur as reactions to overwhelming environmental stress.

   c. Types of mental disorders characterized by lifelong maladaptive patterns of adjustment to life.

   d. A group of disorders with more or less severe disturbances of thought, mood, and/or behavior.

2. From the statements below, select the statement that best differentiates between fear and anxiety.

   a. Fear is a feeling of apprehension caused by a real object in the environment, feeling of apprehension that has no specific object in the environment.

   b. Fear and anxiety produce entirely different physiological reactions.

   c. Fear cannot be controlled, while anxiety can be controlled without the use of drugs.

   d. Fear is a feeling of apprehension that has no specific object in the e anxiety is a feeling of apprehension caused by a real object in the environment.

3. Select the correct definition of the term antianxiety agent.

    a. A drug used to improve the depressed mood of a patient.

    b. A drug used to calm a patient.

    c. A drug which will reduce certain symptoms such as hallucinations and delusions.

    d. A drug which will remove a patient's fear.

4. Select the statement that best describes the use(s) of antidepressant agents.

    a. The treatment of depression that results because of chemical imbalances in the body.

    b. The treatment of depression that is not a result of chemical imbalances in the body.

    c. The treatment of patients who are experiencing periods of overwhelming stress.

    d. The treatment of acute and chronic psychoses.

5. Select the statement that best describes the adverse effects associated with antipsychotic agents.

    a. Antipsychotic agents are noted for the lack of adverse effects they produce.

    b. Antipsychotic agents can cause severe stimulation in many patients.

    c. Antipsychotic agents produce orthostatic hypertension.

    d. Antipsychotic agents can produce reactions that consist of tremors, muscular rigidity, and hypersalivation.

6. Select the statement that best describes the disadvantage(s) of antianxiety agents.

   a. Antianxiety agents can produce drowsiness in patients and can interact with central nervous system (CNS) depressants to produce a greater degree of CNS depression.

   b. Antianxiety agents produce an excessive loss of alertness.

   c. Because of their side effects, overdosage of antianxiety agents frequently results in death.

   d. Antianxiety agents produce tremors, muscular rigidity, and hypersalivation in many patients.

7. From the statements below, select the statement(s) that describes the advantage(s) of antianxiety agents over drugs which were previously used to calm or sedate patients.

   a. Antianxiety agents do not cause excessive loss of alertness.

   b. Antianxiety agents can be safely taken while driving or operating machinery.

   c. Overdosage of antianxiety agents rarely results in death to the patient.

   d. Both a and c.

   e. Both b and c.

8. Select the use of hydroxyzine hydrochloride (Atarax®).

   a. Antidiarrheal agent.

   b. Antianxiety agent.

   c. Antipsychotic agent.

   d. Antipyretic agent.

9. Select the statement that best describes an adverse reaction associated with haloperidol (Haldol®).

   a. This drug may cause extrapyramidal reactions.

   b. This drug may produce hypotension.

   c. This drug may produce overstimulation.

   d. This drug may produce withdrawal.

10. Select the statement which best describes the use(s) associated with chlorpromazine (Thorazine®):

   a. The drug is used to treat acute and chronic types of psychosis.

   b. The drug is used as an antiemetic to prevent pre- or postoperative nausea and vomiting.

   c. The drug is used as an antianxiety agent.

   d. a and b.

   e. b and c.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 9

1. c (para 9-2c)
2. a (para 9-3a, b)
3. b (para 9-3c)
4. b (para 9-11b)
5. d (para 9-18a)
6. a (para 9-8a, b)
7. e (para 9-7a, b)
8. b (para 9-9c)
9. a (para 9-20f)
10. d (para 9-20a)

End of Lesson 9

LESSON ASSIGNMENT

LESSON 10	Central Nervous System (CNS) Stimulants.
TEXT ASSIGNMENT	Paragraphs 10-1--10-9.
LESSON OBJECTIVES	After completing this lesson, you should be able to:

10-1. Given several categories, select the category(ies) of central nervous system (CNS)stimulants.

10-2. Given a group of possible effects, select the pharmacological effect associated with xanthine derivatives.

10-3. Given the trade name of a CNS stimulant and a group of generic names, match the trade name with its generic name.

10-4. Given the trade or generic name of a CNS stimulant and a group of possible clinical uses, side effects, or cautions and warnings, select the clinical use, side effect, or caution and warning associated with that agent.

SUGGESTION After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 10

CENTRAL NERVOUS SYSTEM (CNS) STIMULANTS

Section I. BACKGROUND

10-1. INTRODUCTION TO THE CENTRAL NERVOUS SYSTEM

a. Many people are familiar with the class of drugs known as CNS stimulants. Unfortunately, most people are aware of these agents because of the abuse/misuse associated with these drugs. The central nervous system stimulants do have a variety of medically approved uses. This subcourse lesson will focus on those uses.

b. This lesson will introduce you to the topic of CNS stimulants, how they act, their approved uses, and drugs representative of the drug class. Much has been written on CNS stimulants. If you wish to learn more about these agents, you should obtain an appropriate reference (see the lesson on reference selection, lesson 1 of this subcourse).

10-2. OTHER DRUGS WHICH ACT UPON THE CENTRAL NERVOUS SYSTEM

This lesson will focus on drugs that stimulate the central nervous system. There are, as you know, many classes of drugs that have other effects on the central nervous system. These drug classes include sedative and hypnotic agents (lesson 7), antianxiety agents (lesson 9), and anti-psychotic agents (lesson 9), centrally acting skeletal muscle relaxants (SC MED8O5), and anticonvulsants (lesson 8). You should be familiar with the types of responses produced by these agents because, as you know, patients take a variety of medications. Some combinations of medications may not be desirable.

10-3. CLASSIFICATION OF CENTRAL NERVOUS SYSTEM (STIMULANTS)

a. Central nervous system stimulants excite the nerve cells of the central nervous system. These agents are classified according to their main site of action and their primary pharmacological effects. Following are the three categories of agents:

(1) Cerebral of psychomotor agents.

(2) Analeptics (brain stem stimulants).

(3) Convulsants (spinal cord stimulants).

b. As you might anticipate, when increasingly larger doses of a drug are administered to the patient, the effects produced by the drug cause stimulation of more than one area.

c. Some central nervous system stimulants produce high levels of stimulation at other sites in the body (for example, the heart). In some cases, the usefulness of several CNS agents is limited because of the stimulation they produce in body organs.

Section II. CEREBRAL OR PSYCHOMOTOR AGENTS

10-4. INTRODUCTION

A variety of agents are classified as cerebral or psychomotor central nervous system agents. These drugs have one characteristic in common: they primarily stimulate the cerebral cortex of the brain.

10-5. CLASSES OF CEREBRAL OR PSYCHOMOTOR CENTRAL NERVOUS SYSTEM STIMULANTS

a. **The Xanthine Derivatives**. The xanthine derivatives have several pharmacological effects. One, they directly relax the smooth muscle of the bronchi and pulmonary blood vessels. By such dilation of the bronchi, more oxygen can be drawn into the lungs. Two, they stimulate the central nervous system and produce diuresis (they increase the production of urine) by direct action on the kidney. There are several examples of xanthine derivatives:

(1) Caffeine. Caffeine is found in coffee, tea, and in kola nuts (used to make some soft drinks). Caffeine is a stimulant that has been long used as a morning "picker-upper" for workers and students. Caffeine is found in some headache remedies products promoted to prevent drowsiness, and in some products designed to suppress appetite (in these preparations caffeine acts to stimulate the person). Although caffeine does have some desirable qualities (that is, small doses of the drug can promote better performance on tasks like typing and thinking), it is possible for a person to develop a psychological dependence on the drug. Withdrawal of the drug results in some persons' having mild withdrawal symptoms (for example, headaches).

(2) Aminophylline (Theophylline ethylenediamine). This drug is used in the treatment of bronchial asthma. It is given intravenously to provide rapid relief of pulmonary edema and dyspnea seen in the acute congestive heart failure patient because it increases cardiac output, slightly increases venous pressure, and relaxes the bronchial muscle. Side effects associated with the oral administration of this agent include nausea, vomiting, and nervousness. The patient should be informed to take this medication with food. The medication is supplied in 100 and 200-milligram tablets, 250 and 500-milligram suppositories, and in injectable form (25 milligrams per milliliter in a 10-milliliter ampule).

(3) Theophylline (Theo-dur(®), Elixophyllin(®)). This xanthine derivative is used for the symptomatic relief of asthma because of its bronchial dilation effect. Theolair is but only one of many anhydrous theophylline products in use today. The side effects usually associated with the use of the drug are nausea, vomiting, and nervousness. The patient should be told to take theophylline with food. The drug is usually administered in a dosage of 3 to 5 milligrams per kilogram of body weight. It is supplied in various dosage forms (elixir, tablets, capsules, and sprinkles).

b. **The Amphetamines.** Many health care professionals are concerned about the abuse/misuse of the amphetamines. These Schedule II medications certainly have been abused in the past. Today, physicians and pharmacists cooperate to ensure these drugs are wisely used for medically acceptable purposes. Amphetamines act pharmacologically to produce two primary effects. One, they increase an individual's state of alertness. Two, they elevate a person's mood. Now, several agents will be discussed. The particular use(s) for each agent will be presented.

(1) Methylphenidate (Ritalin(®)). Methylphenidate (Ritalin(®)) is used to treat attention deficit/hyperactivity disorder (ADHD), formerly known as minimal brain dysfunction, and narcolepsy. Observed abnormalities in ADHD include impulsiveness, short attention span, purposeless hyperactivity, emotional overreactivity, coordination and learning deficits, distractibility, and deficits in the perception of space, form, movement, and time. Since the first clinical sign seen with ADHD is purposeless hyperactivity, the terms hyperkinetic and hyperkinesia are sometimes used in place of attention deficit hyperactivity disorder (ADHD). Narcolepsy can be defined as an inability to stay awake. The most common side effect associated with this agent is nervousness. Methylphenidate is a Schedule II drug (Note R). The usual dosage of methylphenidate is 20 to 30 milligrams daily in divided doses. It is supplied in the form of 5 milligram, 10 milligram, and 20-milligram tablets.

(2) Dextroamphetamine sulfate (Dexedrine(®)). Dextroamphetamine was once prescribed as an anoretic (an appetite depressant) for many years. Recently, it has been found that dextroamphetamine's inhibitory effect on the appetite lasts only for four or five weeks. This finding, coupled with its increased abuse, has drastically reduced the quantity of the prescriptions for this drug. This agent is not used in the military for the inhibition of appetite. It is used only for the treatment of attention deficity hyperactivity disorder (ADHD) and narcolepsy. Most military and civilian physicians believe that exercise and the restriction of food (caloric) intake is the method of choice for weight reduction. The most common side effects associated with dextroamphetamine are nervousness and headaches. This drug has a very high abuse potential. It is controlled as a Schedule II (Note R) item. Dextroamphetamine is supplied in 5-milligram tablets, 10- and 15-milligram capsules.

(3) Methamphetamine hydrochloride (Desoxyn(®)). This drug is similar to dextroamphetamine in terms of its ability to suppress the appetite. However, its abuse potential is such that it is rarely used any longer for this purpose.

c. **Other Agents**. Many other drugs produce pharmacological effects similar to those produced by the amphetamines. These are most often used for their ability to suppress the patient's appetite. Sometimes you will find these medications combined with other drugs (for example, a sedative or an antianxiety agent) in order to counteract the stimulation they produce.

(1) Pemoline (Cylert(®)). This drug is used in the treatment of ADHD. It is usually prescribed in a graduated dose, beginning with a 37.5-milligram daily dose. It is then gradually increased at 1-week intervals of 18.75 milligrams until a desired clinical response is observed. The most common side effect seen with this agent is insomnia. Pemoline appears to have a lower abuse potential than methylphenidate; pemoline is classified as a Note Q drug. The drug is supplied in the form of 18.75, 37.5, and 75 milligram tablets.

(2) Diethylpropion hydrochloride (Tenuate(®)). Diethylpropion hydrochloride is used as an appetite suppressant. It is less effective in this use than the amphetamines. It produces such side effects as dryness of the mouth, nausea, and headaches. It is available in both 25-milligram tablets and 75-milligram (timed-release) tablets. Diethylpropion is a Note Q drug.

(3) Phendimetrazine tartrate (Prelu-2(®)). This drug is used as an appetite suppressant. Long-term use of the drug, especially in large doses may, produce psychic dependence. It produces such side effects as nervousness, excitement, euphoria, and dryness of the mouth. It is supplied in 35-mIlligram tablets and capsules and 105 milligram (timed-release) capsules. Phendimetrazine is a Note Q drug.

Section III. ANALEPTIC AGENTS (BRAIN STEM STIMULANTS)

10-6. INTRODUCTION

a. Analeptic agents are drugs that produce two primary effects. One, they stimulate the nerve cells of the body's respiratory center when it has been depressed by some condition (for example, illness or drugs). Two, they stimulate nerve cell centers responsible for keeping a person conscious.

b. Analeptic agents are not commonly used today because of the stimulation they produce in doses sufficient to produce their analeptic effect. These agents can produce such undesirable effects as convulsions, respiratory problems, or vomiting.

10-7. EXAMPLE OF AN ANALEPTIC AGENT

Doxapram (Dopram(®)) is an analeptic agent used for postanesthetic arousal and drug-induced central nervous system depression. It has the ability to arouse the patient after surgery without reducing the analgesia produced by opiates (for example, morphine). Thus, it is used to hasten recovery time. The faster the patient becomes aware of his or her surroundings, the faster nursing personnel are relieved of intensive care responsibilities. Doxapram is also used to stimulate respiration and hasten arousal in patients who have mild to moderate respiratory and central nervous system depression because of overdose. The most common side effects associated with this drug are headaches, nausea, and vomiting. The usual dose of the drug is 0.5 to 2.0 milligrams per kilogram of body weight. It is supplied as an injectable containing 20 milligrams per milliliter of solution.

Section IV. CONVULSANTS (SPINAL CORD STIMULANTS)

10-8. INTRODUCTION

Some chemical substances can so stimulate the motor areas of the central nervous system that a person's muscles begin to powerfully convulse (begin uncontrollable violent contractions). Some natural and manmade chemicals are capable of producing such reactions. For example, tetanospasmin, a chemical produced by the bacteria Clostridium tetani, is such a natural agent. Strychnine, a poison, once was used as a respiratory stimulant; however, its medicinal use has been stopped because of its toxicity.

10-9. THERAPEUTIC USE OF CONVULSANTS

Drugs in this classification have little clinical usefulness. Some drugs in this class have been used in the treatment of some types of psychotic agents.

Continue with Exercises

EXERCISES, LESSON 10

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise. After you have completed all of the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the category(ies) of central nervous system stimulants.

   a. Cerebral agents.

   b. Convulsants.

   c. Analeptics.

   d. All the above.

2. Select the pharmacological effect(s) associated with xanthine derivatives.

   a. Bronchoconstriction.

   b. Smooth muscle relaxation.

   c. Enuresis.

   d. All the above.

SPECIAL INSTRUCTIONS FOR EXERCISES 3 THROUGH 9. Match the generic names below with their corresponding trade names.

3.	Diethylpropion hydrochloride	a.	Dopram(®)
4.	Methyl phenidate	b.	Aminophylline(®)
5.	Theophylline ethylenediamine	c.	Ritalin(®)
6.	Theophylline	d.	Desoxyn(®)
7.	Methamphetamine hydrochloride	e.	Elixophylline(®)
8.	Doxapram	f.	Cylert(®)
9.	Pemoline	g.	Tenuate(®)

10. What is the clinical use of diethylpropion hydrochloride?

    a. Used in the treatment of attention deficit hyperactivity disorder (ADHD).

    b. Used to suppress a patient's appetite.

    c. Used to treat a patient's anxiety.

    d. Used to stimulate a patient's respiratory system.

11. Long-term use of phenmetrazine hydrochloride (Preludin(®)) may produce:

    a. Nausea or vomiting.

    b. Decreased metabolic rate.

    c. Psychic dependence.

    d. Insomnia.

12. What is the clinical use of dextroamphetamine sulfate (Dexedrine(®))?

    a. To suppress a patient's appetite.

    b. To increase a patient's ability to concentrate.

    c. To treat narcolepsy.

    d. To stimulate respiration.

13. When taking Aminophylline orally, the patient should be cautioned:

    a. Not to take the medication with alcohol.

    b. Take the medication with food.

    c. Discontinue the medication immediately if any slight nervousness is detected.

    d. Not to drive while taking the medication.

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 10

1. d (para 10-3a)
2. b (para 10-5a)
3. g (para 10-5c(2))
4. c (para 10-5b(1))
5. b (para 10-5a(2))
6. e (para 10-5a(3))
7. d (para 10-5b(3))
8. a (para 10-5c(2))
9. f (para 10-5c(1))
10. b (para 10-5c(2))
11. c (para 10-5c(3))
12. c (para 10-5a(2))
13. b (para 10-5a(2))

End of Lesson 10

LESSON ASSIGNMENT

LESSON 11 Narcotic Agents.

LESSON ASSIGNMENT Paragraphs 11-1--11-7

LESSON OBJECTIVES After completing this lesson, you should be able to:

11-1. Given a group of definitions, select the definition of analgesia.

11-2. Given a group of pharmacological effects, select those that are produced by narcotic agents.

11-3. Given a group of definitions, select the meaning of the following terms: dysphoria, euphoria, tolerance, and miosis.

11-4. Given a general pharmacological effect produced by the narcotics and a group of statements, select the term that best describes that effect.

11-5. Given several statements, select the statement that best contrasts psychological and physiological dependence.

11-6. Given a group of side effects, select those side effects associated with the narcotic agents.

11-7. Given the trade and/or generic name of a specific narcotic agent, and a list of uses, side effects, or cautions and warnings, select the use, side effect, or caution and warning associated with that agent.

11-8. Given a group of cautions, select the caution associated with the use of narcotic agents.

11-9. Given the name naloxone (Narcan®) and a group of uses/indications, select the use/indication associated with the drug.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.

LESSON 11

NARCOTIC AGENTS

Section I. BACKGROUND

11-1. GENERAL COMMENTS

Most people have legally used narcotic agents. Conditions characterized by a degree of discomfort (that is, pain, diarrhea, or cough), often are treated with medications that have narcotics as the active ingredient. It is very important for all medical personnel to be familiar with narcotic agents.

11-2. HISTORY OF NARCOTIC AGENTS

a. There is evidence that the opium poppy was used in Sumeria as early as 4000 B.C., and it is mentioned in the medical records of ancient Greece and Rome. During the Dark Ages, it passed to the Arabs, who took it to China about 900 A.D. It was either smoked or taken orally.

b. Opium was first used injectably around 1800; the U.S. Civil War saw the first widespread use in this manner. Because of a lack of knowledge and caution, a condition called “Soldier’s Disease” was described--addiction. This coupled with the large influx of Chinese laborers who smoked, and the ready availability of opium caused a great deal of concern. There were no packaging or distribution laws; indeed, a children’s formulation was marketed called “Mrs. Winslow’s Soothing Syrup.” This concern was an important factor in motivation for the Pure Food and Drug Act of 1906.

c. In 1805, a German Pharmacist’s assistant isolated a pure alkaloid (a basic substance found usually in plant parts) from opium that he called morphine. It was subsequently found that opium contains two general categories of alkaloids; narcotics (phenanthrene) such as morphine and codeine, and nonnarcotics (benzylisoquinoline)

11-3. PHARMACOLOGICAL EFFECTS OF THE NARCOTICS

Narcotics produce pharmacological effects when administered to a patient. Some of these effects are desirable, while others are undesirable. Always remember that the legitimate use of these agents is implied in our discussion.

a. **Analgesic Effect.** Analgesia means relief of pain without the loss of consciousness. Analgesia is the most common use of narcotics. Although the exact mechanism of action by which narcotics act is unknown, it is thought that analgesia is obtained by the action of these agents on the cerebral cortex. The relief of pain is enhanced because narcotics raise a patient's pain threshold and thus produce a calming and soothing effect. Narcotic agents have particular application in the relief of continuous, dull pain. Consequently, these drugs are widely used in patients who are terminally ill.

b**. Antitussive Effect.** An antitussive agent acts to control or prevent cough. Some narcotics will depress the cough center of the brain and produce this antitussive effect. In general, the antitussive dose of a narcotic is lower than the analgesic dose of that same drug. Before progressing, it should be noted that a narcotic is not indicated for all types of coughs. Indeed, sometimes it is useful for a patient to cough in order to remove substances from the lungs.

c. **Mood Alteration Effect**. Some narcotics will produce a mood alteration in patients. The types of mood changes can be classified in two categories.

(1) Dysphoria. Dysphoria is a mood alteration characterized by feelings of anxiety, fidgetiness, or being ill at ease.

(2) Euphoria. Euphoria is characterized by an exaggerated feeling of well-being.

d. **Gastrointestinal Effect**. Narcotics produce some significant effects upon the gastrointestinal system (that is, stomach and intestines). Some narcotics are used specifically for their effect upon this system of the body.

(1) Decrease gastrointestinal motility. Narcotics decrease the peristaltic (wavelike) movements of the gastrointestinal tract. Consequently, they may cause constipation. This effect of narcotics is the basis of their being used to treat diarrhea. When used to treat diarrhea, the agents are referred to as antidiarrheals.

(2) Stimulate the chemoreceptor trigger zone. The chemoreceptor trigger zone (CTZ) is located at the base of the brain. When stimulated, the CTZ produces nausea and vomiting. Like many other categories of drugs, narcotics can stimulate the chemoreceptor trigger zone and cause nausea and vomiting.

e. **Respiratory System Effect**. Narcotics cause respiratory system depression because they reduce the sensitivity of the medullary centers to carbon dioxide in the blood. This depression of the respiratory system usually occurs at higher narcotic doses.

11-4. SIDE EFFECTS OF NARCOTICS

Side effects are frequently seen with the use of narcotics. Some of these side effects are characteristics of the narcotic agents.

a. **Dependence.** Dependence is a side effect of narcotics, which has caused much concern among many health-care professionals. There are two types of dependence.

(1) Psychological. Psychological dependence is produced when the drug causes an emotional or mental desire to repeat the use of the drug. Consequently, the individual taking the drug has a craving for the pleasurable mental effects produced by the drug (that is, euphoria, and so forth).

(2) Physiological (physical). Physical dependence is produced by prolonged use of a drug whose pharmacological action causes the body to adapt to its presence. When the drug is withdrawn after the person has become physically dependent, the body of the individual reacts in a hyperexcited way. You have probably read about or seen heroin (narcotic) addicts who are undergoing withdrawal. These episodes of withdrawal are characterized by stimulation of the central nervous system.

b. **Tolerance**. Tolerance is the body's ability to adapt to the presence of a foreign chemical substance (drug). This results in the requirement for progressively larger doses of the drug in order to obtain the same effect in the patient. It should be noted that tolerance is frequently seen in patients who abuse narcotics. Tolerance is not of great concern in narcotic therapy of short duration. However, for those chronically ill patients who are on long-term narcotic therapy, increased doses of the narcotic agents might be indicated to maintain the desired level of analgesia.

c. **Drowsiness**. Drowsiness is another side effect of narcotics. For this reason, individuals who are receiving narcotics should seriously examine their activities (such as driving) for safety purposes.

d. **Miosis**. Miosis (constricted pupils) is an effect commonly known as "pinpoint" pupils. Miosis is commonly seen in patients who are taking narcotic agents.

Section II. NARCOTIC AGENTS AND NARCOTIC ANTAGONISTS

11-5. SPECIFIC NARCOTIC AGENTS

a. **Morphine**. Morphine is the basis of the narcotic effect of opium and is the standard by which other analgesics are judged. It is used in moderate to severe pain, is the analgesic of choice for myocardial infarction, and is used to treat acute pulmonary edema. Morphine is most frequently given IM or SC, 10-15 mg every 4 hours, or IV, where 4-10 mg are diluted and given slowly over 4-5 minutes. It is used less frequently by the oral route (1/15--1/6 the effectiveness of parenteral administration) in a dose of 8-20 mg every 4 hours. The most common side effects associated with morphine are drowsiness, nausea, and vomiting. Morphine is supplied as an injection containing 8, 10, and 15 milligrams per milliliter; in tablets of 10, 15, and 30 milligrams; and as an oral solution containing 10-milligrams per 5-milliliters. Morphine in all forms is a Note R substance.

b. **Codeine**. Codeine is the second naturally occurring narcotic. Its use is very widespread; in some states it can be sold without prescription in combination products if its concentration is weak enough (ETH & codeine, Robitussin AC®). For our purposes, however, when codeine is dispensed as a single agent, it is Note R, when in combination, it is Note Q. Codeine is used as an antitussive, 5-15 mg every 4-6 hours, and as an analgesic in mild to moderate pain, 30-60mg every 4-6 hours. Its most common side effects include drowsiness, nausea/vomiting, and constipation; patients must be cautioned about the drowsiness and the additive effect seen with concurrent use of alcohol. Codeine is available as an injection of 15, 30, and 60 mg/ml, and in 15 and 30 mg tablets. A powder form for compounding is also available.

c. **Hydromorphone (Dilaudid®)**. Hydromorphone (Dilaudid®) is a drug that was obtained by chemical modification of morphine, used as an analgesic in moderate to severe pain. It is frequently used in pain associated with cancer. Its usual dose is 2 mg every 4 to 6 hours. Its major side effects are nausea and vomiting, dizziness, and constipation. Although the manufacturer states that drowsiness occurs infrequently, patients should be made aware of this possibility; also alcohol may intensify its effects. Dilaudid® is a Note R drug and is supplied in tablet or injectable form, both in 1, 2, 3, and 4 mg strengths.

d. **Meperidine (Demerol®)**. Meperidine was the first synthetically produced narcotic. It is one of the first widely used agents for moderate to severe pain. Usual doses of this agent (50-150 mg every 3-4 hours) produce some drowsiness, nausea, and vomiting. Patients who are prescribed meperidine should be cautioned that drowsiness might occur. Further, they should be advised that alcohol might intensify this drowsiness. Meperidine is a Note R drug, which is available as an injection (25, 50, 75, and 100 mg/ml), a tablet (50 or 100 mg tablets), and in a syrup (50 mg/5ml).

e. **Fentanyl (Sublimaze®, Duragesic®, Oralet®, Actiq®)**. Fentanyl is a synthetic agent with actions similar to morphine, but on a weight basis, Sublimaze® is 80-100 times more potent. It is used as an analgesic component in general anesthesia or conscious sedation and given intramuscularly (IM) or intravenously (IV). The dosage is dependent upon its intended role during anesthesia, and ranges from 0.025 to 0.1 mg. Respiratory depression is the side effect of concern for this agent. Fentanyl is unique in that it is available as an injection (Sublimaze®), in a topical patch formulation (Duragesic®), a lozenge (Fentanyl Oralet®) and a lozenge on a stick ["lollipop"[(Actiq®) formulation. The latter three formulations are prescribed primarily for severe pain conditions. Fentanyl is handled as a Note R product.

f. **Methadone (Dolophine®).** Methadone (Dolophine®) is a synthetic agent that has been used as an analgesic for moderate to severe pain and to treat withdrawal symptoms of narcotics in a dose-tapering fashion. The usual dose for analgesia is 2.5-10 mg every 4 hours, and common side effects include drowsiness and nausea or vomiting. The effects of methadone may be intensified by alcohol, and the patient also should be cautioned about drowsiness. The injection, 10 mg/ml, and the tablets, 5 and 10 mg, are all Note R.

g. **Percodan®**. Percodan® is a popular semisynthetic narcotic intended for the relief of moderate pain that contains two salts of oxycodone, combined with aspirin. It is, of course, a fixed combination and is given in a usual dose of one tablet every 6 hours. In addition to the side effects of drowsiness and nausea/vomiting, pruritis is also a fairly frequent complaint. Patient cautionary statements regarding drowsiness and alcohol apply to this agent. It is a Note R product even though it is a combination. Percodan® is available in tablet form, and a half-strength product called Percodan-Demi® is also produced.

NOTE: Combination products of acetaminophen with oxycodone are Tylox® and Percocet®.

h. **Combination Products**. Codeine is combined with aspirin or acetaminophen (Tylenol®) to produce products that are used to treat mild to moderate pain. Common side effects of these combination products include nausea, vomiting, and drowsiness. Patients who are taking these products should be cautioned about the drowsiness. Further, patients should be warned against taking these with alcohol. These combination products are handled as Note Q items.

(1) Empirin® with codeine. Empirin® with codeine is a combination of aspirin and codeine. The usual dosage of these products is from one to two tablets every four hours. The various products are numbered based upon the amount of codeine contained in each product as noted below:

(a) Empirin® with Codeine #2-15 mg of codeine per tablet.

(b) Empirin® with Codeine #3-30 mg of codeine per tablet (most widely used of these products).

(c) Empirin® with Codeine #4-60 mg of codeine per tablet.

(2) Tylenol® with codeine. Tylenol® with codeine is a combination acetaminophen with codeine. The usual dosage of these products is from one to two tablets every four hours. As with Empirin® with codeine, the products are numbered based upon the amount of codeine contained in each tablet as noted below:

(a) Tylenol® with Codeine #1-7.5 mg of codeine per tablet.

(b) Tylenol® with Codeine #2-15 mg of codeine per tablet.

(c) Tylenol® with Codeine #3-30 mg of codeine per tablet (most widely used of these products).

(d) Tylenol® with Codeine #4-60 mg of codeine per tablet.

11-6. CAUTIONS OF NARCOTIC USE

a. Narcotics should not be used in patients experiencing any form of respiratory depression (that is, asthma).

b. Narcotics cause an increase in intracranial pressure (pressure within the skull). Therefore, they should not be used in the presence of head injuries.

c. Narcotics should be used cautiously in combination with other drugs that depress the central nervous system.

11-7. NARCOTIC ANTAGONISM

a. **Explanation**. As previously mentioned, narcotics depress the respiratory system. Sometimes it is necessary to reverse this respiratory depression (that is, overdose of narcotics) in order to save a patient's life.

b. **Naloxone (Narcan®)**. Naloxone (Narcan®) is the only true narcotic antagonist in that it does not possess agonist or morphine-like properties and, most importantly, it has no respiratory depressant action in therapeutic doses. Because it does not depress respiration, naloxone is the drug of choice in the treatment of respiratory depression of unknown causes, but which is suspected of being produced by a narcotic. Narcan® is given in a usual dose of 0.4 mg IM, SC, or IV, and may produce some nausea and vomiting. It is not a controlled substance and is available as an injection, 0.4 mg/ml or 0.2 mg/ml, for pediatric use.

c. **Indications/Uses**. Naloxone (Narcan®) is indicated/used to reverse respiratory depression caused by natural and synthetic narcotics, pentazocine (Talwin®), and propoxyphene (Darvon®). It is not effective against the respiratory depression caused by the barbiturates or benzodiazepines. Naloxone is a competitive antagonist.

Continue with Exercises

EXERCISES, LESSON 11

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the group of definitions below, select the meaning of the term analgesia.

   a. The decrease in a patient's pain threshold.

   b. The relief of pain with loss of consciousness.

   c. The relief of pain without the loss of consciousness.

   d. The loss of consciousness with no effect on pain level.

2. From the group of pharmacological effects below, select the response that contains those produced by narcotic agents.

   (1) Relief of pain.
   (2) Antitussive.
   (3) Antipyretic.
   (4) Decrease gastrointestinal motility
   (5) Produce diarrhea.
   (6) Depress respiratory rate.
   (7) Increase blood pressure.
   (8) Increase respiratory rate.
   (9) Decrease clotting time.
   (10) Produce loss of consciousness.

   a. (1), (2), (3), (6) and (10).

   b. (1), (2), (4) and (6).

   c. (1), (2) and (5).

   d. (1), (2), (4), (5), (6), (7) and (10).

3. From the group of definitions below, select the meaning of the term euphoria.

   a. A mood alteration characterized by feelings of anxiety.

   b. A mood alteration characterized by feelings of being ill at ease.

   c. A mood alteration effect characterized by analgesia.

   d. A mood alteration characterized by exaggerated feelings of well-being.

4. Narcotic agents produce an effect on a patient's respiratory system. From the list of descriptions below, select the best description of the specific effect produced by the narcotic agents.

   a. Narcotic agents stimulate a patient's respiratory system.

   b. Narcotic agents depress a patient's respiratory system.

   c. Narcotic agents decrease the levels of carbon dioxide in the blood.

   d. Narcotic agents depress the respiratory rate only in small doses.

5. Narcotic agents produce an effect on a patient's gastrointestinal system. From the list of descriptions below, select the best description of that specific effect.

   a. Narcotic agents stimulate the patient's CTZ to produce nausea and vomiting.

   b. Narcotic agents stimulate the patient's CTZ to produce diarrhea.

   c. Narcotic agents stimulate the patient's CTZ to produce constipation.

   d. Narcotic agents stimulate the patient's CTZ to produce peristalsis.

6. From the group of side effects below, select the response that contains the side effects associated with the narcotic agents.

(1)	Independence.	(4)	Miosis.
(2)	Mitosis.	(5)	Dependence.
(3)	Tolerance.	(6)	Drowsiness.

a. (1), (2), (3), (6).

b. (1), (3), (5), (6).

c. (3), (4), (5), (6).

d. (1), (2), (5), (6).

7. From the definitions below, select the best definition of the term tolerance.

a. The ability of the body to adapt to the presence of foreign substances that result in the requirement for progressively larger doses of the drug to obtain the same effect.

b. The ability of the body to adapt to the presence of foreign substances that result in the requirement for progressively smaller doses of the drug to obtain the same effect.

c. The ability of the body to adapt to the presence of foreign substances that result in the requirement for changing the route of administration of the drug.

d. The ability of the body to adapt to the presence of foreign substances that result in the requirement for changing the dosage form of the drug.

8. From the list of uses below, select the use of codeine.

a. Antitussive.

b. Antiemetic.

c. Antipyretic.

d. Sedative.

9. From the list of uses below, select the use of hydromorphone (Dilaudid®).

    a. Analgesic for moderate to severe pain.

    b. Analgesic for mild to moderate pain.

    c. Antidiarrheal in severe diarrhea.

    d. Emetic in poisoning.

10. From the list of cautions and warnings, select the caution and warning associated with the use of meperidine hydrochloride (Demerol®).

    a. The patient should be cautioned against taking aspirin with meperidine.

    b. The patient should be warned that alcohol can intensify the drowsiness caused by meperidine.

    c. The patient should be warned against not taking the drug on a regular basis.

    d. The patient should be cautioned against exercise when taking the drug.

11. From the list of uses below, select the use associated with methadone (Dolophine®).

    a. An agent used to treat withdrawal symptoms associated with narcotic antagonists.

    b. An agent used in the treatment of mild to moderate pain.

    c. An agent used in the treatment of alcohol withdrawal symptoms.

    d. An agent used in the treatment of the withdrawal symptoms associated with narcotic agents.

12. From the group of cautions below, select the caution associated with the use of narcotic agents.

    a. Narcotics should not be administered to patients over the age of 65.

    b. Narcotics should not be administered intravenously.

    c. Narcotics should be used cautiously with drugs that depress the central nervous system.

    d. Narcotics should not be used by cardiac patients.

13. Select the use of naloxone (Narcan®) from the list below.

    a. Narcotic.

    b. Narcotic analgesic.

    c. Narcotic suppressant.

    d. Narcotic antagonist

Check Your Answers on Next Page

SOLUTIONS TO EXERCISES, LESSON 11

1. c (para 11-3a)
2. b (paras 11-3a, b, d(1), e)
3. d (para 11-2c(2))
4. b (para 11-3e)
5. a (para 11-3d(2))
6. c (paras 11-4a, b, c, d)
7. a (para 11-4b)
8. a (para 11-5b)
9. a (para 11-5c)
10. b (para 11-5d)
11. d (para 11-5f)
12. c (para 11-6c)
13. d (para 11-7b)

End of Lesson 11

ANNEX

DRUG PRONUNCIATION GUIDE

This Drug Pronunciation Guide was developed to help you to learn how the trade and generic names of commonly prescribed medications are frequently pronounced. Not all the drugs in the guide are discussed in this subcourse. Remember, it is not enough to be able to know the uses, indications, cautions and warnings, and contraindications for a drug--you must also know how to pronounce that drug's name.

Trade Name	***Generic Name***
A	
Actifed (Ak'-ti-fed)	Triprolidine (Tri-pro'-li-deen) and Pseudoephedrine (Soo-do-e-fed'-rin)
Adapin (Ad'-a-pin)	Doxepin (Dok'-se-pin)
Sinequan (Sin'-a-kwan)	" "
Afrin (Af'-rin)	Oxymetazoline (Ok-see-met-az'-o-leen)
Aldactazide (Al-dak'-ta-zide)	Spironolactone (Spi-ro-no-lak'-tone) and Hydrochlorothiazide (Hy-dro-klor-thi'-a-zide)
Aldactone (Al-dak'-tone)	Spironolactone (Spi-ro-no-lak'-tone)
Aldomet (Al'-do-met)	Methyldopa (Meth-il-do'-pah)
Alupent (Al'-u-pent)	Metaproterenol (Met-a-pro-ter'-eh-nol)
Amoxil (Am-ok'-sil)	Amoxicillin (Ah-moks'-i-sil-in)
Amphojel (Am'-fo-jel)	Aluminum (Al-loo'-mi-num) Hydroxide (Hy-drok'-side)
Ampicillin (Amp'-I-sil-in)	Same
Antepar (Ab'-te-par)	Piperazine (Pi-per'-ah-zeen)
Anturane (An'-tu-rain)	Sulfinpyrazone (Sul-fin-pie'-ra-zone)
Anusol (An'-u-sol)	Pramoxine (Pram-ok'-seen)
Apresoline (A-press'-o-leen)	Hydralazine (Hy-dral'-ah-zeen)
Aralen (Ar'-a-len)	Chloroquine (Klor'-o-kwin)
Aristocort (A-ris'-to-cort)	Triamcinolone (Tri-am-sin'-o-lone)
Artane (Ar'-tane)	Trihexyphenidyl(Tri-hek-see-fen'-i-dil)
A.S.A.	Aspirin (As'-per-in)
Atromid S (A'-tro-mid)	Clofibrate (Klo-fi'-brate)
Avlosulfon (Av-lo-sul'-fon)	Dapsone (Dap'-sone)
Azolid (Az'-o-lid)	Phenylbutazone (Fen-il-bute'-a-zone)
B	
Bactrim (Bak'-trim)	Sulfamethoxazole (Sul-fah-meth-oks'-ah-zole) and Trimethoprim (Tri-meth'-o-prim)
Bellergal (Bel'-er-gal)	Ergotamine (Er-got'-a-meen), Phenobarbital (Feen-o-bar'-bi-tal) and Belladonna (Bel-la-don'-na) Alkaloids

Trade Name	*Generic Name*
Benadryl (Ben'-a-dril)	Diphenhydramine (Di-fen-hy'-dra-meen)
Bendectin (Ben-dek'-tin)	Doxylamine (Dok-sil'-a-meen)
Benemid (Ben'-eh-mid)	Probenecid (Pro-ben'-eh-sid)
Bonine (Bo'-neen)	Meclizine (Mek'-li-zeen)
C	
Cafergot (Kaf'-er-got)	Ergotamine (Er-got'-a-meen) and Caffeine (Kaf'-feen)
Calamine (Kal'-a-mine)	Same
Catapres (Kat'-a-press)	Clonidine (Klo'-ni-deen)
CeeNu (See'-new)	Lomustine (Lo-mus'-teen)
Chlor-Trimeton (Klo-tri '-meh-ton)	Chlorpheniramine (Klor-fen-it'-a-meen)
Clomid (Klo'-mid)	Clomiphene (Klo'-mi-feen)
Clonopin (Klo-o-pin)	Clonazepam (Klo-na'-ze-pam)
Codeine (Ko'-deen)	Same
Cogentin (Ko-jen'-tin)	Benztropine (Benz'-tro-peen)
Colace (Ko'-lace)	Dioctyl(Di-ok'-til) Sodium (So'-dee-um) Sulfosuccinate (Sul-fo-suk'-si-nate)
Colchicine (Kol'-chi-seen)	Same
Compazine (Kom'-pa-zeen)	Prochiorperazine (Pro-klor-per'-a-zeen)
Cordran (Kor'-dran)	Flurandrenolide (Floor-an-dren'-o-lide)
Coumadin (Koo'-mah-din)	Warfarin (War'-fah-rin)
CP	Cloroquine (Klor'-o-kwin) and Primaquine (Prim'-a-kwin)
Cyclogyl (Si'-klo-jel)	Cyclopentolate (Si-klo-pen'-to-late)
Cytomel (Si'-to-mel)	Liothyronine (Li-o-thy-ro-neen)
Cytoxan (Si-tok'-san)	Cyclophosphamide (Si-klo-fos'-fa-mide)
D	
Dalmane (Dal '-mane)	Flurazepam (Floor-az'-e-pam)
Darvocet (Dar'-vo-set)	Propoxyphene (Pro-pok'-se-feen) and Acetaminopen (As-et-am'-ino-fen)
Darvon (Dar'-von)	Propoxyphene (Pro-pok-se-feen)
Decadron (Dek'-a-dron)	Dexamethasone (Dek-sa-meth'-ah-sone)
Deltasone (Del '-ta-sone)	Prednisone (Pred'-ni-sone)
Demerol (Dem'-er-ol)	Meperidine (Meh-pair'-i-deen)
Dexedrine (Deks '-eh-dreen)	Dextroamphetamine (Deks-tro-am-fet'-a-meen)
Diabinese (Di-ab'-i-nees)	Chlorpropamide (Klor-prop'-a-mide)
Diethylstilbestrol (Di-eth-il-stil-bes'-trol)	Same
Dilantin (Di-lan'-tin)	Phenytoin (Fen'-i-toin)
Dilaudid (Di-law'-did)	Hydromorphone (Hy-dro-more' -fon)
Dimetane (Di'-meh-tane)	Brompheniramine (Brom-fen-ir'-a-meen)

Trade Name	*Generic Name*
Dimetapp (Di‘-meh-tap)	Brompheniramine (Brom-fen-ir’-a-meen) Phenylephrine (Fen-il-ef’-rin) and Phenylpropanolamine (Fen-il-pro-pan-ol‘-a-meen)
Disophrol (Dice’-o-frol)	Dexbrompheniramine (Deks-brom-fen-ir‘-a-meen) and Pseudoephedrine (Soo-do-e-fed‘-rin)
Dolophine (Dol‘-o-feen)	Methadone (Meth’-a-done)
Domeboro (Dome-bor’-o)	Aluminum (Ah-loo’-mi-num) Acetate (As‘-e-tate)
Donnatal (Don’-na-tal)	Belladonna (Bel-la-don’-na) Alkaloids (Al’-ka-loids) and Phenobarbital (Feen-o-barb’-i-tal)
Doxidan (Dok’-si-dan)	Danthron (Dan’-thron) and Dicctyl (Di-ok’-til) Calcium (Kal‘-see-um) Sulfosuccinate (Sul-fo-suk’-si-nate)
Drixoral (Driks’-or-al)	Dexbrompheniramine (Deks-brom-fen-ir’-a-meen) and Pseudoephedrine (Soo-do-e-fed‘-rin)
Dulcolax (Dul’-ko-laks)	Bisacodyl (Bis-a’-ko-dil)
Dyazine (Di’-a-zide)	Triamterene (Tri-am’-ter-een) and Hydrochlorothiazide (Hy-dro-klor-o-thi‘-a-zide)
Dymelor (Die’-meh-lor)	Acetohexamide (As-e-to-heks’-a-mide)
Dyrenium (Die-ren’-i-um)	Triamterene (Tri-am’-ter-een)
E	
Efudex (Ef'-u-deks)	Fluorouracil (Floo-ro-ur’-ah-sil)
Elavil (El’-ah-vil)	Amitriptyline (Am-i-trip’-til-een)
Elixir Terpin (Ter’-pin) Hydrate	Same
Empirin (Em’-per-in)	Codeine (Ko’-deen) and Aspirin (As’-per-in)
E-Mycin (E-mie’-sin)	Erythromycin (E-rith-ro-mie’-sin)
Equanil (Ek’-wa-nil)	Meprobamate (Me-pro-bam’-ate)
Ergomar (Er’-go-mar)	Ergotamine (Er-got’-a-meen)
Ergotrate (Er’-go-trate)	Ergonovine (Er-go-no’-veen)
Erythrocin (Er-eeth’-ro-sin)	Erythromycin (Er-eeth-ro-my’-sin) Stearate (Stare’-rate)
Esidrix (Es’-i-driks)	Hyrochlorothiazide (Hy-dro-klor-o-thi‘-a-zide)
F	
Feosol (Fe’-o-sol)	Ferrous (Fer’-rus) Sulfate (Sul’-fate)
Fergon (Fer’-gon)	Ferrous (Fer’-rus) Gluconate (Glu'-con-ate)

Trade Name	*Generic Name*
Fiorinal (Fee-or'-i-nal)	Butalbi tal (Bu-tal'-bi-tal), Apririn, Phenacetin (Fen-ass'-eh-tin), and Caffeine (Kaf'-feen)
Flagyl (Fla'-jil)	Metronidazole (Me-tro-ni'-dah-zole)
Flexeril (Flek'-sa-ril)	Cyclobenzaprine (Si-klo-benz'-a-preen)
Fulvicin (Ful'-vi-sin)	Griseofulvin (Griz-e-o-ful'-vin)
G	
Guantanol (Gan'-ta-nol)	Suiphamethoxazole (Sul-fah-meth-oks'-ah-zole)
Gantrisin (Gan'-tri-sin)	Sulfisoxazole (Sul-fi-sok'-sah-zole)
Gelusil (Jel'-u-sil)	Aluminum (Ah-loo'-mi-num) Hydroxide (Hy-drok'-side) and Magnesium (Mag-nee'-zee-um) Hydroxide
Grifulvin (Gri-ful'-vin)	Griseofulvin (Griz-e-o-ful'-vin)
Gynergen (Jin'-er-jen)	Ergotamine (Er-got'-a-meen)
H	
Haldol (Hal'-dol)	Haloperidol (Hal-o-pair'-i-dol)
Halotestin (Hal-o-tes'-tin)	Fluoxymesterone (Floo-ok-see-mes-teh-rone)
Hexadrol (Hek'-sa-drol)	Dexamethasone (Dek-sa-meth'-a-sone)
Hydrodiuril (Hy-dro-di'-ur-il)	Hydroclorothiazide (Hy-dro-kior-thi'-a-zide)
Hygroton (Hy-grow'-ton)	Chiorthalidone (Kior-thal'-i-done)
I	
Ilosone (I'-low-sone)	Erythromycin (Er-ith-ro-mi'-sin) Estolate (Es'-to-late)
Inderal (In'-der-al)	Propranolol (Pro-pran'-o-lol)
Indocin (In'-do-sin)	Indomethacin (In-do-meth'-a-sin)
INH	Isoniazid (I-so-ni'-a-zid)
Insulin (In'-sul-in)	Same
Intal	Cromolyn (Kro'-mo-lin)
Ismelin (Is'-meh-lin)	Guanethidine (Gwan-eth'-i-dine)
Isopto-Atropine (I-sop-to-at'-ro-peen)	Atropine (At'-ro-peen)
Isopto-Carpine (I-sop-to-car'-peen)	Pilocarpine (Pile-o-car'-peen)
Isordil (I'-sor-dil)	Isosorbide (I-so-sor'-bide)
J-K	
Keflex (Kef'-lex)	Cephalexin (Sef-ah-lek'-sin)
L	
Lanoxin (Lan-ok'-sin)	Digoxin (Di-jok'-sin)
Larodopa (Lar-o-do'-pa)	Levodopa (Le-o-do'-pa)
Larotid (Lar'-o-tid)	Amoxicillin (Ah-moks'-i-sil-in)
Lasix (La'-siks)	Furosemide (Fu-ro'-se-mide)
Leukeran (Lu'-ker-an)	Chlorambucil (Klor-ram'-bu-sil)

Trade Name	*Generic Name*
Librium (Lib'-ree-um)	Chlordiazepoxide (Klor-die-az-eh-pok'-side)
Lidex (Lie'-deks)	Fluocinoide (Floo-o-sin'-o-nide)
Lomotil (Lo'-mo-til)	Diphenoxylate (Die-fen-ok'-si-late)
Lopressor (Lo'-pres-sor)	Metoprolol (Met-o-pro'-lol)
Lotrimin (Lo'-tri-min)	Chlotrimazole (Klo-trim'-ah-zole)
M	
Maalox (May'-loks)	Aluminum (Ah-loo'-mi-num) and Magnesium (Mag-nee'-zee-um) Hydroxides
Macrodanton (Ma-kro-dan'-tin)	Nitrofurantoin (Ni-tro-fur-an'-toin)
Mandelamine (Man-del'-a-meen)	Methenamine (Meth-en'-a-meen) Mandelate (Man'-deh-late)
Medihaler-Iso (Med-i-hail-er-I'-so)	Isoproterenol (I-so-pro-ter'-en-ol)
Mellaril (Mel'-la-ril)	Thioridazine (Thi-o-rid'-a-zeen)
Metamucil (Met-a-mu'-sil)	Psyllium (Sil'-e-um)
Metaprel (Meh'-ta-prel)	Metaproterenol (Meh'-ta-pro-ter'-eh-nol)
Methotrexate (Meth-o-treks'-ate)	Amethopterin (Ah-meth-op'-ter-in)
Milk of Magnesia	Same
Minipress (Min'-i-press)	Prazosin (Pra'-zo-sin)
Minocin (Min'-o-sin)	Minocycline (Mi-no-si'-kleen)
Monistat (Mon'-i-stat)	Miconazole (Mi-kon'-ah-zole)
Motrin (Mo'-trin)	Ibuprofen (I-bu'-pro-fen)
Myambutol (My-am'-bu-tol)	Ethambutol (Eth-am'-bu-tol)
Mycostatin (My-co-stat'-in)	Nystatin (Ny-stat'-in)
Mylanta (My-lan'-ta)	Aluminum (Ah-loo'-mi-num) and Magnesium (Mag-nee'-zee-um) Hydroxides and Simethicone (Si-meth'-i-kone)
Myleran (My-ler-an)	Busulfan (Bu-sul'-fan)
Mylicon (My'-li-kon)	Simethicone (Si-meth'-i-kone)
Mysoline (My'-so-leen)	Primidone (Pri'-mi-done)
N	
Nalfon (Nal'-fon)	Fenoprofen (Fen-o-pro'-fen)
Naprosyn (Na'-pro-sin)	Naproxen (Na-prok'-sen)
Nembutal (Nem'-bu-tal)	Pentobarbital (Pen-to-barb'-i-tal)
Neosynephrine (Nee-o-sin-eh'-frin)	Phenylephrine (Fen-il-eh'-frin)
Nitrobid (Ni'-tro-bid)	Nitroglycerin (Ni-tro-gli'-ser-in)
Nitrol (Ni'-trol)	"
Nitrostat (Ni-tro-stat)	"
Noctec (Nok'-tek)	Chloral Hydrate (Klor'-al- Hy'-drate)
Norfiex (Nor'-fleks)	Orphenadrine Citrate (Or-fen'-a-dreen)
Norpace (Nor'-pace)	Disopyramide (Di-so-peer'-a-mide)

Trade Name	*Generic Name*
Novahistine (No-va-his'-teen) Expectorant	Guaifenesin (Gwi-fen'-eh-sin), Phenylpropanolamine (Fen-il-pro-pan-ol'-a-meen), and Codeine (Ko'-deen)
NTG	Nitroclycerin (Ni-tro-gli'-ser-in)
Nupercainal (New-per-kain'-al)	Dibucaine (Die'-bu-kain)
O	
Oretic (O-ret'-ik)	Hydrochiorothiazide (Hy-dro-kior-thi'-a-zide)
Orinase (Or'-in-ase)	Tolbutamide (Tol-bu'-tah-mide)
Ornade (Or'-nade)	Chlorpheniramine (Klor-fen-ir'-a-meen), Triprolidine (Tri-pro-li-deen) and Pseudoephedrine (Su-do-eh-fed'-rin)
P	
Parafon Forte (Pair'-a-fon For'-tay)	Chlorzoxazone (Klor-zok'-sa-zone)
Percodan (Per'-ko-dan)	Oxycodone (Ok-si-ko'-done)
Periactin (Per-ee-ak'-tin)	Cyproheptadine (Si-pro-hep'-tah-deen)
Persantine (Per-san'-teen)	Dipyridamole (Di-pi-rid'-ah-mole)
Phenobarbital (Feen-o-barb'-it-al)	Same
Phenylpropanolamine (Fen-il-pro-pan-ol'-a-meen)	Same
Pitocin (Pi-tow'-sin)	Oxytocin (Ok-see-tow'-sin)
Pontocaine (Pon'-to-kain)	Tetracaine (Teh'-tra-kain)
Povan (Po'-van)	Pyrvinium (Pire-vin'-ee-um)
Premarin (Prem'-ar-in)	Conjugated (Kon'-joo-gay-ted) Estrogens (Es-tro-jens)
Presamine (Press'-a-meen)	Imipramine (Im-ip'-rah-meen)
Primaquine (Pri'-mah-kwin)	Same
Probanthine (Pro-ban'-theen)	Propantheline (Pro-pan'-the-leen)
Pronestyl (Pro-nes'-til)	Procainamide (Pro-kain'-a-mide)
Prophylthiouracil (Pro-pil-thi-o-u'-rah-sil)	Same
Prostaphlin (Pro-staff'-lin)	Oxacillin (Oks'-ah-sil-in)
Provera (Pro-ver'-ah)	Medroxyprogesterone (Med-rok-see-pro-jes'-ter-one)
Pyridium (Pie-rid'-ee-um)	Phenazopyridine (Fen-ahs-o-per'-i-deen)
Q	
Quinidine (Kwin'-i-deen)	Same
Quinine (Kwie'-nine)	Same
R	
Reserpine (Ree-ser'-peen)	Same
Retin A (Reh'-tin A)	Tretinoin (Tret'-i-noin)
Rifadin (Rie-fad'-in)	Rifampin (Rie-fam'-pin)
Riopan (Rie'-o-pan)	Magaidrate (Mag'-al-drate)

Trade Name	*Generic Name*
Rimactane (Rim-act'-ane)	Rifampin (Rie-fam'-pin)
Ritalin (Rit'-a-lin)	Methylphenidate (Meth-il-fen'-i-date)
Robaxin (Ro-bak'-sin)	Methocarbamol (Meth-o-kar'-ba-mol)
Robitussin (Row-i-tus'-sin)	Guaifenesin (Gwie-fen'-eh-sin)
Robitussin DM	Guiafenesin and Dextromethorphan (Dek-tro-meh-or'-fan)
S	
Sansert (San'-sert)	Methysergide (Meth-ee-ser'-jide)
Seconal (Sek'-o-nal)	Secobarbital (Sek-o-bar'-bi-tal)
Selsun (Sel'-sun)	Selenium (Se-leh'-nee-um)
Septra (Sep'-tra)	Sulfamethoxazole (Sul-fah-meth-oks'-a-zole) and Trimethroprim (Tri-meth'-o-prim)
Serax (See'-raks)	Oxazepam (Oks-az'-eh-pam)
Silvadene (Sil'-va-deen)	Silver Sulfadiazine (Sul-fa-die'-a-zeen)
Sinemet (Si'-ne-met)	Levodopa (Le-vo-do'-pa)
Sinequan (Sin'-a-kwan)	Doxepin (Dok'-seh-pin)
Sorbitrate (Sor'-bi-trate)	Isosorbide (I-so-sor'-bide)
Stelazine (Stel'-a-zeen)	Trifluoperazine(Tri-floo-o-per'-a-zeen)
Sudafed (Soo'-da-fed)	Pseudophedrine (Soo-do-eh-feh'-drin)
Sulamyd (Sul'-a-mid)	Sulfacetamide (Sul-fah-set'-a-mide)
Sulfamylon (Sul-fa-mie'-lon)	Mafenide (Maf'-eh-nide)
Sultrin (Sul'-trin)	Sulfathiazole (Sul-fah-thi'-ah-zole) Sulfacetamide (Sul-fah-set'-ah-mide) and Sulfabenzamide (Sul-fah-benz'-ah-mide)
Surfak (Sur'-fak)	Dioctyl (Di-ok'-til) Calcium (Kal'-see-um) Sulfosuccinate (Sul-fo-suk'-si-nate)
Synalar (Sine'-a-lar)	Fluocinolone (Floo-o-sin'-o-lone)
Synthroid (Sin'-throid)	Levothyroxine (Lee-vo-thi-rok'-sin)
T	
Tace (Tace)	Chlorotrianisene (Klor-o-tri-an'-I-seen)
Tagamet (Tag'-a-met)	Cimetidine (Si-met'-i-deen)
Talwin (Tal'-win)	Pentazocine (Pen-taz'-o-seen)
Tandearil (Tan'-da-ril)	Oxyphenbutazone (Ok-see-fen-bute'-a-zone)
Tegretol (Teg'-reh-tol)	Carbamazepine (Kar-ba-maz'-eh-peen)
Tessalon (Tess'-a-lon)	Benzonatate (Benz-on'-a-tate)
Tetracycline (Tet-ra-si'-kleen)	
Thorazine (Thor'-a-zeen)	Chlorpromazine (Klor-pro'-ma-zeen)
Thyroid (Thy'-roid)	Same
Tigan (Tie'-gan)	Trimethobenzamide (Tri-meth-o-benz'-a-mide)
Timoptic (Tim-op'-tic)	Timilol (Tim'-o-lol)

Trade Name	*Generic Name*
Tinactin (Tin-act'-in)	Tolnaftate (Tol-naf'-tate)
Titralac (Ti'-tra-lak)	Calcium (Kal-see-um) Carbonate (Kar'-bon-ate) and Glycine (Gly'-seen)
Tofranil (Toe'-fra-nil)	Imipramine (I-mip'-rah-meen)
Tolectin (Tow-lek'-tin)	Tolmetin (Tol-met'-in)
Triavil (Tri'-a-vil)	Perphenazine (Per-fen'-a-zeen) and Amitriptlyline (Am-i-trip'-ti-leen)
Trilafon (Try'-la-fon)	Perphenazine (Per-fen-a-zeen)
Tylenol (Tie'-leh-nol)	Acetaminophen (As-et-am'-ino-fen)
Tylenol #3	Acetaminophen and Codeine (Ko'-deen)
U	
Unipen (U'-ni-pen)	Nafcillin (Naf-sil-lin)
Urecholine (Ur-eh-ko'-leen)	Bethanecol (Beth-an'-eh-kol)
V	
Valisone (Val'-i-sone)	Betamethasone (Beh-tah-meth'-a-sone)
Valium (Val'-ee-um)	Diazepam (Die-aze-eh-pam)
Vermox (Ver'-moks)	Mebendazole (Meh-ben'-dah-zole)
Vibramycin (Vie-bra-my'-sin)	Doxycycline (Doks-see-si'-kleen)
W-X	
Xylocaine (Zie'-low-kain)	Lidocaine (Lie-do-kain)
Y-Z	
Zarontin (Zar-on'-tin)	Ethosuximide (Eh-tho-suks'-a-mide)
Zyloprim (Zie'-low-prim)	Allopurinol (Al-lo-pure'-in-ol)

End of Annex